EXTRADURAL HÆMATOMA
OBSERVATIONS ON 125 CASES

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THE problems of extradural hæmorrhage have exercised the minds of surgeons for more than a century. As early as 1816 Charles Bell published the results of some remarkably prescient experiments in which he showed that, when the cadaver skull was struck by a mallet with sufficient force to "shake loose" the dura and then dye was injected into the carotid artery, the dye would collect in the extradural space.

Jacobson's classical description (1885) of middle-meningeal hæmorrhage was based on a series of 71 cases of which 10 survived, giving a mortality rate of 86%. This appears to have been the first indication that survival might be possible after extradural hæmorrhage, and the clinical picture of the condition became widely recognised. Nevertheless the mortality of extradural hæmorrhage has remained formidably high through the years despite the evolution of modern surgery and neurosurgery.

Since the early part of the 1939–45 war there has developed an increasing interest in head injuries in general and the problem of extradural hæmorrhage in particular.

Woodhall et al. (1941) collected 177 reported cases with a mortality of 66%. Munro and Maltby (1941) recorded a personal series of 44 cases with a 55% mortality. Gallagher and Browder (1950) reported 100 cases with a 46% mortality. Schneider and Tytus (1955) stated that in the U.S.A. mortality figures between 30% and 50% were widely accepted.

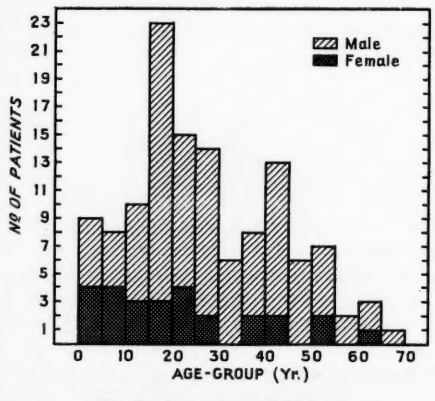

Fig. 1—Age and sex distribution.

Hooper (1959) listed the mortality figures of seventeen series of cases published between 1941 and 1959. These figures varied from 76% (Larghero 1951) to 5% (Sartorius and Humphries 1946). Hooper's own mortality figure for a personal series of 83 cases was 23%. There are no published series of cases exceeding 40 with a mortality-rate of less than 20% (Lewin 1954).

Material

We present here a series of 125 cases of traumatic extradural hæmorrhage. All were admitted under the care of one of us (W. McK.) between 1940 and 1959 to the department of neurosurgery of St. George's Hospital (Atkinson Morley's Hospital), or The Hospital for Sick Children, Great Ormond Street, or The National Hospital, Queen Square; and all were transferred from other hospitals. These 125 cases represent 3% of all the head injuries admitted to these departments during this period.

Age and Sex Distribution

The age-distribution for both sexes is shown in fig. 1. It can be seen that the usual preponderance of males does not obtain in the pædiatric age group. There were 27 females and 98 males, the median age being 24 years.

TABLE I—TABLE OF ACCIDENTS

Type of accident	No. of cases	% of total	No. dead
Direct blow to head	16	13	3
Fall from standing position	14	11	2
Fall from roof or ladder	10	8	5
Fall out of cot or baby high-chair	4	3	0
Fall down stairs	8	6	3
Road traffic accidents:			
Pedestrians	17	44	3
Pedal-cyclists	16		6
Motor-cyclists	16		6
In automobile	6		3
War injuries	8	6	0
Unknown	10	8	3

Nature of Trauma

The types of accident responsible for this series are set out in table I which shows the number of cases of each type, together with its percentage incidence, and the number dead. Table I shows that road traffic accidents form by far the largest group (44%).

Clinical Picture and Evolution

The often-described story of initial loss of consciousness followed by a lucid interval, with subsequent lapse into coma as cerebral compression increases, is uncommon and was seen in only 27% of the patients in this series. It has been found appropriate, after reviewing the histories of our patients, to divide them into groups in respect of changes in level of consciousness observed in the evolution of the condition.

Group 1 (10 cases): patients who sustained no initial loss of consciousness and who remained fully conscious until time of treatment.

Group 2 (17 cases): patients who sustained no initial loss of consciousness but who subsequently became unconscious and remained so until time of treatment.

Group 3 (35 cases): patients who were initially unconscious but recovered and remained alert or relatively so until time of treatment.

Group 4 (33 cases): patients who were initially unconscious, recovered for a "lucid interval", and subsequently lost consciousness again.

Group 5 (30 cases): patients who were unconscious from the outset and did not at any time regain their senses before treatment.

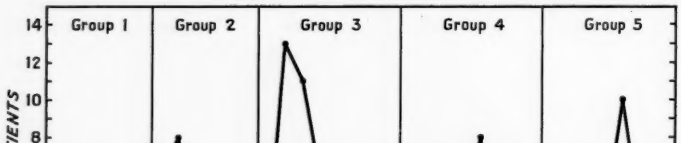

Fig. 2—Comparative curves representing age-distribution in each of the five clinical groups.

Relation of Clinical Groups to Age

In group 1 no fewer than 7 patients (70%) were under the age of 15 years and none was more than 25 years of age. Group-2 cases share a low age-distribution with group 1, 11 of the patients (65%) being under the age of 15 years and none over 27 years. This group is especially interesting in that it contains the highest proportion of the very young, 4 patients being under 2 years of age and 1 aged 4 years. On the other hand in group 5, 17 patients (57%) were over 40 years of age, only 1 being less than 15 years of age. Group 3 contains the largest number of patients and consists mainly of young adults. Only 3 cases were under the age of 15 years and 2 were over the age of 40. Group-4 patients in our series presented with the " lucid interval " picture. They numbered 33, making 27% of the total. The age-distribution is weighted by the older patients, though less so than group 5, 11 of the patients (32%) being over the age of 40 and 5 being under the age of 15. These facts are more clearly expressed in graphic form in fig. 2.

Clinical Features

When considering symptoms and signs it will be appreciated that the majority of patients had disturbances of consciousness and were unable to complain.

Disturbances of consciousness.—Depression of level of consciousness of varying degree occurred in 112 (90%) of the patients. Such depression varied from drowsiness to deep coma. All patients have been placed into one of four arbitrarily chosen " strata of consciousness " at time of operation or treatment—namely (*a*) alert (13 patients), (*b*) drowsy (33 patients), (*c*) stuporose (37 patients), (*d*) comatose (42 patients). It will be shown later that this stratification has considerable prognostic significance (Munro and Maltby 1941, Hooper 1959).

Scalp injury.—Local bruising and laceration of the scalp were present in the majority of cases and were usually, but not invariably, located over the hæmatoma.

Eye signs.—Much the most important of numerous eye signs found was the development of pupillary inequality, dilatation, and fixation. Such pupillary abnormalities were seen in 74 patients. In addition, various degrees of palsy of the third, fourth, and sixth cranial nerves were found. In 63 cases the ipsilateral pupil was much dilated, or dilated and fixed. In 11 cases the pupils were unequal, the larger one being contralateral to the hæmatoma; but in all of these the inequality was slight and in no case was a frankly dilated pupil seen contralateral to the lesion. 4 patients with bilaterally fixed and dilated pupils on admission survived, their ages being 1, 2, 27, and 41 years. 6 patients had complete palsy of the third cranial nerve, which in 5 was ipsilateral and in 1 contralateral; this last case was of slow development, the hæmatoma being of thirteen days' duration when the patient was admitted. Isolated sixth-nerve palsies (all ipsilateral) were seen in 7 patients. Conjugate deviation of the eyes (to the opposite side in every case) was seen in 7 patients.

These figures confirm the accuracy of pupillary dilatation as a localising sign in extradural hæmorrhage, and compare with those found in a recent series of cases of subdural hæmatoma, in which dilatation of the ipsilateral pupil was seen in 90% of cases of unilateral hæmatomas with pupillary dilatation (McKissock, Richardson, and Bloom 1960).

Papillœdema.—Swelling of the optic discs was noted in 18 cases. The earliest was at six hours after injury; but the majority were slowly developing cases, and in 9 this sign was found more than seven days after injury.

Other localising signs.—Dysphasia was found in 8 patients, all of whom had left-sided hæmatomas. 2 patients presented with homonymous hemianopia, both contralateral to the lesion and correctly localising. It is now well established that hemisphere compression by an extrinsic lesion such as subdural or extradural hæmatoma may cause homonymous hemianopia. The possible mechanisms involved have been discussed by Meyer (1920) and Pevehouse, Bloom, and McKissock (1960).

Limb paresis or other pyramidal-tract signs were present in 85 cases—in 81 cases contralateral and in 4 ipsilateral. These 4 ipsilateral hemipareses were all in slowly developing cases of more than seven days' duration, and again comparison with the incidence of ipsilateral hemiparesis of 30% in chronic subdural hæmatoma is of interest (McKissock et al. 1960).

Headache.—40 patients complained of headache. In 5 of these the pain was unilateral and on the side of the lesion.

Vomiting.—Vomiting was a prominent feature in 28 patients. Of these, 18 were under 15 years of age—i.e., 67% of the total number of children.

Epilepsy.—In only 5 cases were convulsive seizures seen. These were generalised in 3 and focal in 2.

Systemic signs.—Bradycardia, defined as a pulse-rate of 60 per minute or less in adults, was noted in 57 cases, but slowing to some point above 60 was common. Severe respiratory disturbances, such as stertor or periodicity, were found in 18 cases, 3 of whom stopped breathing altogether before operation.

Signs of blood-loss—i.e., intense pallor, tachycardia, and hypotension—were found in 4 cases, all infants. These were closed head injuries, and in all there was a large quantity of blood in the extradural space.

Special Investigations

Lumbar Puncture

This procedure was carried out in only 15 patients. The pressure ranged from 120 to 430 mm. of water, and in 4 cases was less than 200 mm. of water. The validity of pressure readings at lumbar puncture in the acute head injury is questionable, and the presence or absence of red blood-cells in the cerebrospinal fluid has little significance. The risk of precipitating a pressure cone, however, is

considerable and lumbar puncture is not considered an appropriate investigation in suspected extradural hæmatoma.

Skull Radiography

Fracture.—Many of the patients presented too urgent a surgical problem to allow for time in the X-ray department, and only 96 of the 125 had preoperative skull X-rays. In 82 cases fractures were demonstrated and a suture diastasis was seen in 3. Of the 11 radiologically negative cases, 2 were shown subsequently to have fractures at postmortem examination, the remaining 9 having no fracture demonstrated either at operation or postmortem. Of the 29 cases not X-rayed, 19 were found to have fractures either at operation or postmortem examination.

Absence of fracture.—Excluding the patients who were not X-rayed the incidence of extradural hæmorrhage without skull fracture in this series is 9 out of 96 (9%). If one accepts evidence other than radiological for absence of a fracture, then the incidence is 19 out of 125 (19%). The true incidence no doubt lies between these two figures.

The occurrence of extradural hæmorrhage without skull fracture is generally thought to be rare but is nevertheless well documented. Mealey (1960) points out that the majority of such cases reported have been young. Of the nine certain cases in our series the ages were as follows: $3^1/_2$, $4^1/_2$, 9, 9, 10, 20, 25, 29, and 33 years—i.e., over half were under 15 years of age.

Pineal displacement.—In 11 cases the pineal body was calcified, and in 8 of these it was displaced 3–9 mm. away from the midline. It is important to note that in the 3 cases in which the pineal body was in the midline significant temporal extradural hæmatomas were present.

Ventriculography.—It has been our policy to perform ventriculography when a surface hæmatoma is suspected and not revealed by exploratory burrholes. In this series the procedure was carried out on 26 occasions, the lesion being demonstrated in every case.

Carotid angiography.—This investigation was carried out in only 6 patients. Features of the carotid angiogram which are characteristic of extradural hæmatoma (Norman 1956) were present in 4 of the 6. 2 showed displacement of the superior sagittal sinus away from the vault and 2 an extracerebral space-occupying lesion causing concavity of the surface of the hemisphere soon after the injury. The other two angiograms merely indicated a space-occupying lesion situated in temporal and subtemporal regions. Our experience of carotid angiography in the diagnosis of extradural hæmatoma is small, and we are therefore unable to express strong views about its merits in these lesions. This question has been discussed by Irsigler (1958).

Situation of Hæmatoma

By far the commonest location for extradural hæmatoma is the temporal fossa, bleeding having apparently arisen from the middle meningeal artery or its branches in 83% of our cases. However, it is not unusual for hæmatomas to form in other situations. In this series the hæmatomas were placed as follows: temporal, 100; frontal, 9; parietal or parieto-occipital, 11; posterior fossa, 5. 3 cases were bilateral: 1 bifrontal; 1 bitemporal; and the 3rd biparietal, the bleeding arising in this case from the superior sagittal sinus. Thus fully 20% of the hæmatomas were located outside the temporal fossa, and posterior-fossa hæmatomas formed 4% of the total.

TABLE II—TREATMENT IN 125 CASES

Treatment	Children	Adults	Total
Died before operation	0	8	8
Conservative	0	1	1
Operation	27	89	116
Total	27	98	125

Treatment

Of the 125 cases in the series, operation was carried out in 116. 1 patient was clinically well, the diagnosis being made by carotid angiography; this patient was treated conservatively and made a good recovery. 8 patients died before operation, 2 of them succumbing within a few minutes of admission (table II).

Technique

The principle of an exploratory burrhole over the hæmatoma, with subsequent enlargement by craniectomy to an opening fully adequate for its evacuation and the achievement of hæmostasis, is thoroughly established. This technique was followed in all cases but 3, which were submitted to formal craniotomy. The bleeding-point responsible for the hæmatoma was apparent in 43 of the operations, as follows: middle meningeal artery or its branches, 35 cases; superior sagittal sinus, 2 cases; lateral sinus, 3 cases; diploe, 3 cases.

The dura bleeds diffusely as a result of its stripping by the hæmatoma, and hæmostasis may be difficult and time-consuming. However, drainage of the extradural space was very rarely necessary. Because of an appreciable incidence of associated subdural hæmatoma, a small opening was made in the dura for inspection of the subdural space, any collection therein being dealt with. The subdural space was then filled with physiological-saline solution to lift the depressed dura to the surface, where it was held with stitches to surrounding muscle and pericranium. The tentorium was in no case incised.

Since the great majority of extradural hæmatomas are in the middle fossa, temporal burrholes will in most cases discover the lesion. Localising factors such as scalp injury, fractures, and neurological signs are, of course, always taken into account when sitting a burrhole. However, the incidence of atypically situated hæmatomas is such that a negative exploratory burrhole must not be taken as evidence against the diagnosis. It is a not uncommon experience that a burrhole which is as little as 1 cm. away from the edge of an extradural hæmatoma of considerable size may show no indication of its presence. The only sure way of locating or excluding the hæmatoma which is not revealed by exploratory burrholes is to make unhesitating use of special investigations—ventriculography or carotid angiography, usually the former. This has been our rule and part of our mortality is the result of failing to adhere to this policy.

Associated Lesions

Subdural hæmatoma.—In 12 of our cases there was present a concomitant subdural hæmatoma—ipsilateral in 8, contralateral in 2, and bilateral in 2 cases.

Intracerebral hæmatoma.—2 intracerebral hæmatomas were encountered, both in the temporal lobe. 1 was associated with an ipsilateral subdural hæmatoma, the extradural clot, which was not found, being situated in the posterior fossa. The other was associated with ipsilateral subdural and extradural hæmatomas; only the extradural clot was found.

Errors in Management

Lesion missed at operation.—This is a most important group of 7 cases, illustrating the worst mistakes in management. Some of these patients should not have died. In 1 case in which the patient did not survive and in which multiple exploratory burrholes had been made, necropsy showed the fatal hæmatoma midway between frontal and temporal burrholes, both of which had failed to demonstrate the lesion. In 2 more, bilateral exploratory burrholes in parietal and temporal regions were made but failed to uncover a frontal hæmatoma. In 2, biparietal burrholes only were made, postmortem examination subsequently revealing a massive temporal hæmatoma; failure to make temporal burrholes was fatal here. In 1 case a subdural hæmatoma was encountered overlying an intracerebral hæmatoma, both of which were evacuated. After death an unsuspected posterior-fossa extradural hæmatoma was found. In 5 of these patients, ventriculography would have ensured diagnosis and further exploration at the appropriate site. The 7th patient did, in fact, undergo ventriculography but died before further action could be taken; postmortem examination showed a left middle-fossa hæmatoma.

Coexisting lethal lesion missed at operation.—There were 3 patients who died after evacuation of an extradural hæmatoma and who were shown at necropsy to have unsuspected major coexisting lesions. 1 patient, who had a right temporal extradural clot removed, had also left temporal-fossa extradural and subdural hæmatomas. 1 case had bilateral subdural hæmatomas undiscovered; and a 3rd patient had a contralateral subdural hæmatoma. Ipsilateral subdural hæmatomas should be found at routine opening of the dura at operation. Contralateral hæmatomas, subdural or extradural, may be missed without adequate, bilateral burrhole exploration in every case. Again we stress that suspicion of such a lesion, which cannot be found by burrhole exploration, indicates ventriculography or carotid angiography.

Inadequate operation.—Only 2 cases who died postoperatively were found to have significant extradural blood-clot still present at postmortem examination. Both patients died shortly after operation, and it must be conceded that the procedure was technically inadequate in respect of either evacuation of the hæmatoma or achievement of hæmostasis.

TABLE III—DATA ON 34 DEATHS

Groups	No. of cases	Postmortem findings
Dead before operation ..	8	Middle-fossa extradural hæmatoma: 5 Posterior-fossa extradural hæmatoma with bilateral subdural hæmatomas: 1 Posterior-fossa extradural hæmatoma: 1 Occipital and posterior-fossa extradural hæmatoma: 1
Negative exploration ..	7	Frontal extradural hæmatoma: 3 Temporal extradural hæmatoma: 3 Posterior-fossa extradural hæmatoma with associated supratentorial subdural hæmatoma and intracerebral hæmatoma: 1
Hæmatoma dealt with but coexisting lesion missed	3	Bilateral extradural and subdural hæmatomas: 1 Bilateral subdural hæmatomas: 1 Contralateral subdural hæmatoma: 1
Operation inadequate ..	2	Significant, compressing extradural blood-clot still present
Irreversible brain damage not compatible with survival	11	Hemisphere pulping, massive œdema, widespread intracerebral bleeding, tentorial and medullary pressure-cones, hæmorrhages in midbrain and brainstem
Death from extracranial complications	2	Pulmonary embolism: 1 "Stove-in" chest with pulmonary œdema: 1
Cause of death unknown after operation	1	No postmortem examination

Mortality and Postmortem Findings

The overall mortality of the series, including those patients who did not reach operation, was 34 (27%). The surgical mortality was 26 out of 116 operations (23%).

The 34 deaths (table III) are best considered in groups, some of which have already been discussed. They are set out below in table form.

Fate of Survivors

The eventual fate of survivors from extradural hæmorrhage is very poorly documented in the extensive literature on this subject. Lewin (1949) described the late results in 26 cases of extradural hæmatoma, all of whom had returned to full work or school within 2 years.

All cases in our series have been or will be followed up indefinitely. Of the 91 survivors, 63 have recovered and are back to full employment, school, or normal occupation. The 28 patients who have not achieved full rehabilitation are described in table IV.

TABLE IV—LATE DISABILITY IN 28 CASES WITHOUT FULL REHABILITATION

Degree of disability	No. of patients	Nature of disability	Occupation
Total physical disablement	4	Aphasia, hemiplegia, severe mental retardation in children (2)	Not employable
Total intellectual disablement	4	Gross memory impairment, personality disturbance, chronic alcoholism	Not employable
Partial physical disablement	16	Hemiparesis, dysphasia, ocular palsies, uniocular blindness	Part-time or sheltered employment
Epilepsy ..	4	Post-traumatic major epilepsy	Sheltered employment

Subjective symptoms such as persistent headache, dizzy spells, paræsthesæ of limbs, slight dysphasia, and limb weakness are common and tend to improve steadily with time. There were 2 epileptic patients besides those in the table, who sustained their head injury during a seizure and who continued to have fits afterwards. The rate of post-traumatic epilepsy is perhaps surprisingly low—4 out of 91 (4·3%). Some patients may, of course, develop epilepsy in the future.

Of the 91 survivors 8 (9%) were totally disabled and unable to work. These figures may be compared with those cited by Rowbotham et al. (1954), who found that of 236 consecutive cases of head injury of all kinds 10 (4%) were unable to work at the time of follow-up approximately four years later. Thus, despite the severity of the lesion, survivors from extradural hæmatoma have a relatively good prognosis.

Extradural Hæmatoma in Children

In this series there were 27 patients under the age of 15 years, representing 22% of the total; 6 of them were infants less than 2 years of age. These children presented certain characteristic clinical features. Fully 18 (67%) of them sustained no initial loss of consciousness, compared with only 9 out of 98 adults. On the other hand, 16 of them were unconscious at the time of operation. Thus the majority presented the picture which has been described as the "latent interval" (Ingraham et al. 1949)—i.e., not initially unconscious but progressing, sometimes in a fluctuating manner, through drowsiness to stupor and then coma. Only 6 adults presented this sequence.

TABLE V—INTERVALS BETWEEN INJURY AND OPERATION IN CHILDREN AND ADULTS

Interval from injury to operation	No. of children	No. of adults
Less than 24 hr.	10 (37%)	52 (58%)
1–6 days	11 (41%)	23 (26%)
7–13 days	4 (15%)	10 (11%)
14 days or more	2 (7%)	4 (5%)
Total	27 (100%)	89 (100%)

The rate of evolution of the clinical picture in children tended to be somewhat slower than in adults. The intervals between injury and operation for children and for adults are compared in table v.

It can be seen that significantly more children than adults came to operation after the first twenty-four-hour period—perhaps because of a higher incidence of venous bleeding from the diploe. The relation of the rate of development of the hæmatoma to prognosis is discussed in detail later.

Vomiting was a prominent symptom in children, occurring in 18 cases, compared with only 10 out of 98 adults.

Blood-loss

It is not perhaps sufficiently well recognised that an infant may lose a significant fraction of his blood-volume into the extradural space while exhibiting relatively little neurological disturbance. Signs of severe blood-loss, found in 4 of our infants with closed head injuries, should be considered an important factor in favour of the diagnosis of extradural hæmorrhage. The hæmoglobin level should always be estimated.

Absence of Skull Fracture

5 of the children in this series who were X-rayed presented no skull fracture or suture diastasis. This

TABLE VI—MORTALITY RELATED TO LEVELS OF CONSCIOUSNESS AT TIME OF OPERATION IN 116 CASES

Level of consciousness	No. of cases	No. of deaths	
Alert	13	0	
Drowsy	33	3 (9%)	(10%)
Stuporose	37	5 (14%)	
Comatose	33	18 (55%)	(33%)

represents an incidence of at least 21% in patients under the age of 15 years, compared with 4% in the adult group. This relatively high proportion of children with extradural hæmatoma who have no skull fracture has been noted by others. Ingraham et al. (1949) reported that skull fracture was absent in 8 out of 20 cases. The suggested explanation is the elasticity of the bones of the cranial vault and the open suture-lines in the child's skull. The anatomical studies of children's skulls by Campbell and Cohen (1951) are relevant to this argument. These workers translated Charles Bell's idea into the more modern concept of differing coefficients of elasticity of dura and bone causing a shearing stress at the junction of the layers, with resulting separation.

Mortality in Children

Of the 27 children 2 died, giving a mortality of 7%. No patient under the age of 7 years died. This low mortality-rate conforms with that of Ingraham and Matson (1954), in whose series 3 out of 30 children died.

Discussion

FACTORS IN PROGNOSIS

On reviewing this material the following prognostic factors become apparent: (1) level of consciousness at time of operation, (2) age, (3) rate of evolution of the clinical picture.

Level of Consciousness at Time of Operation

The influence of this factor is expressed in table VI, which shows the mortality-rate for each of the strata of consciousness previously referred to (these figures are calculated for the 116 surgical cases).

The very significant difference in prognosis between the first three levels taken together and the comatose patients is clear. This is doubtless due to the severity of associated brain injury related to coma. The 55% mortality figure for comatose patients corresponds closely with the 57% mortality-rate for " group-5 " cases. Other workers have made similar observations. Munro and Maltby (1941) and Hooper (1959) divided their patients into three

TABLE VII—MORTALITY RELATED TO LEVEL OF CONSCIOUSNESS AT TIME OF OPERATION

—	Munro and Maltby 1941	Hooper 1959	Present series
Alert ..	17%	0%	0%
Drowsy ..	46%	12%	9%
Comatose ..	71%	35%	33%

TABLE VIII—MORTALITY RELATED TO LEVELS OF CONSCIOUSNESS (ROWBOTHAM ET AL. 1954)

Level of consciousness	No. of cases	No. of deaths
Confused to semiconscious ..	724	27 (3%)
Semicomatose	101	27 (27%)
Comatose	175	121 (69%)

groups in respect of level of consciousness. Taking our " stupor " and " coma " categories together to correspond approximately with the third category of these workers, their mortality-rate figures may be compared as in table VII.

It is of interest to compare these figures with the mortality-rates given by Rowbotham et al. (1954) in their analysis of 1000 consecutive head injuries of all types in adults, grouped similarly according to level of consciousness (table VIII).

It can be seen that the prognosis of the comatose case of extradural hæmorrhage is little better than the prognosis of comatose head injuries in general; again the severity of primary brain injury is presumably the factor responsible.

Age

The correlation of age with death-rate is demonstrated clearly in fig. 3. Of 10 children under the age of 7 years none died. No patient over the age of 60 years survived.

Rate of Evolution of Clinical Picture

It is well known that some extradural hæmatomas are slow in developing, the adjectives " subacute " and " chronic " having been used by some workers (Imler and Skultety 1954, Trowbridge et al. 1954), and that these delayed cases have a better prognosis than the acute. The significance of rate of evolution of the

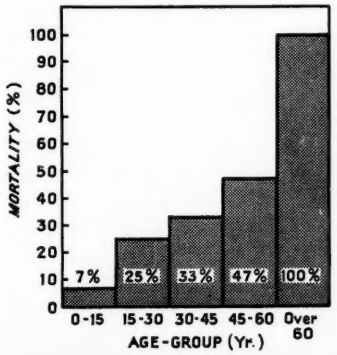

Fig. 3—Correlation of age-groups with mortality.

TABLE IX—INTERVAL BETWEEN INJURY AND OPERATION RELATED TO MORTALITY

Interval between injury and operation	No. of patients	No. of deaths
Up to 24 hr.	62	19 (30%)
25 hr. to 6 days	34	5 (17%)
7–13 days	14	2 (14%) (13%)
14 days or more	6	0 (0%)

TABLE X—MORTALITY RELATED TO CLINICAL GROUPS

Group	No. of cases	No. of deaths
1 (always conscious)	10	0 (0%)
2 (initially conscious; became unconscious)	17	5 (29%)
3 (initially unconscious; became conscious)	35	3 (8%)
4 (lucid interval)	33	9 (27%)
5 (never conscious)	30	17 (57%)

hæmatoma is clearly demonstrated in this series by table IX.

It can be seen that mortality is highest in the most acute cases which come to operation within twenty-four hours. Thereafter follows a sharp drop in mortality, which nevertheless remains appreciable until the end of the second week. The longest period between injury and operation was thirty-one days. Of the cases which presented within the first twenty-four-hour period, mortality-rate varied little with interval between injury and operation.

As was stated in the introduction to this paper, there is no published series of cases larger than 40 with a mortality of less than 20%. The fact that the prognosis of a given case of extradural hæmorrhage depends on a number of factors, some of which are independent of the surgeon, has been shown in our own series. Mortality figures cited for small series of cases are therefore unacceptable since there might well be a weighting by types of case with an inherently good or bad prognosis. A good example is the series of Sartorius and Humphries (1946), who reported 5% mortality in 20 cases. To illustrate this argument, the various mortality-rates for each of the five clinical groups, described earlier, are shown in table X.

AVOIDABLE DEATHS

The earliest possible diagnosis and the most urgent possible surgical treatment are the only measures which will effectively reduce what is still an excessively high mortality. The difficulties in diagnosis are doubtless made greater by the standard clinical undergraduate teaching on extradural hæmorrhage which emphasise the picture of the "lucid interval" and tends to disregard the finding of most writers on this subject—namely, that this variety of clinical presentation is found in only a minority of cases. In this series it accounted for 33 (27%) of the 125 cases. Once the possibility of an extradural hæmatoma is considered, then all possible measures must be taken to find or exclude it with certainty. Such measures include adequate burrhole exploration and the use of special techniques such as ventriculography and carotid angiography.

Hooper (1959) considers that "a mortality rate of 10% should be regarded as a reasonable figure in centres where neurosurgical facilities exist". We have carefully reviewed our own mortality and calculate that 15 of the patients who died might have survived had no mistakes in management been made. Subtracting this figure from the true mortality, a theoretical mortality-rate of 15% for the whole series and of 12% for the surgical cases should have been achieved. The application of this calculation to each of the five clinical groups separately produces the figures in table XI.

TABLE XI—ACTUAL MORTALITY AND LOWEST POSSIBLE MORTALITY RELATED TO CLINICAL GROUPS

Group	Actual mortality (%)	Lowest possible mortality (%)
1	0	0
2	29	6
3	8	6
4	27	5
5	57	47

Comparison of these actual and theoretical mortality figures shows that the greatest "wastage" was in groups 2 and 4. The severe mortality of group-5 cases is little influenced.

All the patients were transferred from other hospitals without special neurosurgical facilities. No doubt earlier diagnosis and referral to our care would have saved further cases. Nevertheless, it seems that in the best possible circumstances there must be an inevitable mortality, to which the main contributor is the "group-5" type of case which has an inherently bad prognosis. We believe with Hooper that this inevitable mortality should be in the region of 10%.

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THE SYNDROME OF MAGNESIUM DEFICIENCY IN MAN

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DESPITE several reports of hypomagnesæmia in man (Martin et al. 1952, Flink et al. 1954, Potts and Roberts 1958, Randall et al. 1959), the clinical syndrome resulting from pure magnesium deficiency has not been clearly delineated, because nearly all the cases had other biochemical abnormalities. We therefore now present the clinical and metabolic findings in three patients with pure magnesium deficiency.

THE FIRST CASE

Previous History

The patient was a man of 33, who had been quite well until 1956, when diarrhœa started. He passed about five motions

a day, which were pale, soft, and bulky. He was admitted to University College Hospital in March, 1957, under the care of Prof. C. E. Dent, and the diagnosis of idiopathic steatorrhœa was confirmed. At the time it was not thought practical to keep him on a gluten-free diet. His clinical condition remained excellent, but the diarrhœa persisted until December, 1958, when acute intestinal obstruction supervened. Laparotomy showed this was due to a kink in a widely dilated piece of small bowel. The kink was freed, and a mesenteric lymph-node biopsy was taken: this was normal. A month later, at a second laparotomy, a perforated jejunum was found. Paralytic ileus ensued, and persisted for 6 weeks. When the patient had recovered, a gluten-free diet was started: this reduced the severity of the diarrhœa. In March, 1959, however, he was readmitted to University College Hospital complaining of severe cramps, vertigo, and staggering. Attacks of typical spontaneous tetany were observed: the serum-calcium was 3·8 mEq. per litre and the serum-potassium 3·0 mEq. per litre. Vitamin-D therapy and extra potassium chloride were started, but he proved very resistant to vitamin D, and not until 15 mg. (600,000 units) calciferol per day was given by mouth did the serum-calcium level reach normal values. At this stage (June, 1959) he had normal calcium and potassium levels, but he still felt dizzy and unsteady, and he showed a positive Chvostek sign. For this reason a sample of serum was sent to us for magnesium estimation: this contained 0·20 mEq. per litre (compared with a normal range of 1·50–1·80 mEq. per litre [Alcock et al. 1960]). The patient's condition continued to deteriorate rapidly, and he was transferred to Hammersmith Hospital for studies of magnesium metabolism.

The Magnesium-deficiency Syndrome

At this time the patient passed one or two loose bowel motions per day. His main complaints were of vertigo on suddenly changing position, and especially on lying down when he said " the bed rises up to the ceiling ", and of weakness. He looked ill and pale. His abdomen was distended, with a large ventral hernia, but without tenderness or palpable masses. There was a mild degree of symmetrical wasting of the muscles of the shoulder girdle, arms, and pelvic girdle. Muscle-tone was normal. He was somewhat unsteady when walking but showed no evidence of ataxia when lying down. All sensory modalities were normal. The tendon reflexes of the arms and quadriceps were obtained only with reinforcement. The achilles-tendon reflexes were absent. Abdominal reflexes were present, and the plantar responses were flexor. Chvostek's sign was readily elicited, but Trousseau's test was consistently negative after 8 minutes. No involuntary movements or tremors were seen.

Investigations (other than calcium and magnesium) revealed:

Blood.—Serum-inorganic-phosphate 2·5 mg. per 100 ml.; alkaline phosphatase 1·6 King-Armstrong units; sodium 143, potassium 3·1–4·4, and plasma-CO_2 content 30 mEq. per litre; urea 26 mg. per 100 ml.; hæmoglobin 13·0 g. per 100 ml.; and white-cell count 3600 per c.mm., with 49% neutrophils.

Urine.—Glucose was absent, and aminoacids were present in normal amounts, but a small amount of phosphoethanolamine was detected. 94% of an oral water-load of 1 litre was excreted in 4 hours.

Radiographs of the chest and skeleton were normal; electrocardiograms (E.C.G.s) showed low-voltage and flat T waves (fig. 1); the electroencephalogram (E.E.G.) was normal; the basal metabolic rate was −21%; and a bone biopsy from the iliac crest showed narrow trabeculæ but no osteoid seams.

Therapy and Progress

During the initial balance, the patient's symptoms and signs remained unchanged until the 12th day, when he suddenly became confused and disorientated. This was accompanied by vomiting and followed by two convulsive seizures. An intravenous infusion of magnesium chloride 100 mEq. in 1 litre 5% dextrose was given over the next 4 hours, after which Chvostek's sign became negative for the first time, the left achilles-tendon reflex was present, and the voltage of the E.C.G.

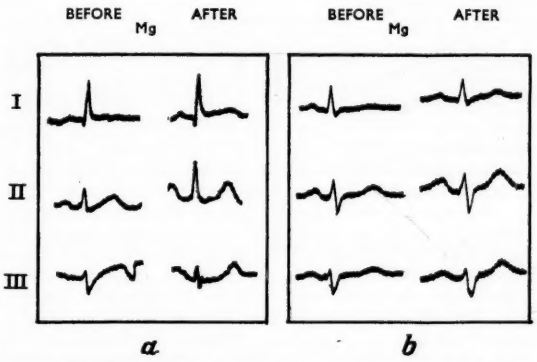

Fig. 1—E.C.G.s before and after magnesium therapy: (*a*) case 3; and (*b*) case 1.

was increased. Over the next day his confusion gradually receded, and a left homonymous hemianopia became evident along with some motor dysphasia, perseveration, and slight right-sided weakness and inattention. An E.E.G. showed on the left side large delta waves replacing the alpha rhythm.

All these neurological signs gradually disappeared over the next 5 days, leaving some slight euphoria. He had complete amnesia for the convulsive seizures and the day following them. After the emergency magnesium-chloride therapy, further magnesium was given as intramuscular and oral supplements as described under " Metabolic Studies in the First Case ". On this regime the patient's strength improved rapidly, and within a fortnight he walked with greater confidence and steadiness than for several months. His diarrhœa became much less severe. The tendon reflexes were now all present, though sluggish. The plasma-alkaline-phosphatase had risen to 3·2 K.A. units by the 8th day of magnesium therapy.

Cortisone (150 mg. per 24 hours) was later added to the therapy, without further obvious benefit. The patient was discharged 6 weeks after admission, feeling very well, and taking supplements of magnesium (which provided 200 mEq. per 24 hours), smaller amounts of potassium and calcium, prednisone (10 mg. per 24 hours), and a gluten-free diet. No further vitamin D has been given. He has remained very fit on this regime, but when the magnesium supplements were withheld for a week, the plasma-magnesium fell from 2·0 to 0·9 mEq. per litre, he felt weaker, the diarrhœa became worse, and Chvostek's sign reappeared. He has therefore continued to take magnesium supplements.

THE SECOND CASE

A 58-year-old woman had hyperparathyroidism with severe bone-disease but without renal failure. At operation a parathyroid adenoma was removed. Tetany appeared on the 5th postoperative day and was controlled by calcium gluconate intravenously. At about the same time she became depressed, irritable, and hostile, resenting any disturbance. All her muscles became weak and she had slight dysarthria and a coarse tremor. The tendon reflexes were normal. These signs persisted for 6 days, despite large doses of calcium which controlled her tetany. On the 11th postoperative day her serum-calcium was 4·4 mEq. per litre and serum-magnesium was 1·0 mEq. per litre. There was no tetany. An intravenous infusion of magnesium chloride 100 mEq. was given over 4 hours. After this the patient's mental state improved strikingly; she was cheerful and talkative for the first time. Muscle power improved considerably, and the dysarthria and tremor disappeared. An E.C.G. taken 5 hours after the end of the magnesium infusion showed a slight increase in voltage. Magnesium supplements were then given by mouth, and the intravenous calcium therapy discontinued. Tetany reappeared on the 16th postoperative day, when the serum-calcium was 3·8 mEq. per litre, and the serum-magnesium 2·0 mEq. per litre.

THE THIRD CASE

A woman of 38 was admitted in semicoma after a urinary infection. She had renal failure due to renal tubular acidosis and chronic pyelonephritis. Because of osteomalacia she had been taking calciferol by mouth in doses of 100,000–600,000 international units per day. On treatment with antibiotics, blood-transfusion, and intravenous sodium lactate her condition improved until the 6th day of admission, when she had a generalised epileptiform convulsion. Chvostek's sign was then positive, and the tendon reflexes were all sluggish. The serum-electrolytes (mEq. per litre) were: magnesium 0·9, sodium 143, potassium 5·3, CO_2 content 27, and calcium 4·7, and the urea was 130 mg. per 100 ml. An E.C.G. showed low voltage of all complexes. An intravenous infusion of magnesium chloride 50 mEq. was given over 4 hours. At the end of this infusion the patient said she felt much better and stronger, and she was much more cheerful. Chvostek's sign was negative, and an E.C.G. taken 45 minutes after the end of the magnesium infusion showed a definite increase in voltage of the QRS complex and T waves (fig. 1). 8 hours after the infusion the serum electrolytes (mEq. per litre) were: magnesium 2·0, sodium 133, CO_2 content 24, and calcium 6·6; and the urea was 120 mg. per 100 ml.

METABOLIC STUDIES IN THE FIRST CASE

The calcium and magnesium metabolic data are shown in fig. 2.

Methods

Balance studies for calcium and magnesium were made in the metabolic unit. For each regime studied, after an equilibration period of 5 days, fæces were collected in two- or three-day pools and processed by the method of King and Wootton (1956).*

Samples of diet and fæces were ashed and dissolved as described by MacIntyre and Davidsson (1958). Plasma was deproteinised by the perchloric acid/phosphate mixture (MacIntyre 1957). Calcium and magnesium were determined by flame-spectrophotometer at the 422·7 mμ and 285·2 mμ lines respectively.

Initial Basal Data

Throughout the studies the patient had the same basic daily diet containing 15 mEq. magnesium and 8 mEq. calcium. Initially the diet was supplemented by 114 mEq. calcium gluconate orally, which was reduced after the convulsions to 38 mEq. The magnesium supplements are detailed below. Initially, calciferol (15 mg. per day) was given.

On admission the patient's plasma-calcium was 5·0 mEq. and plasma-magnesium 0·2 mEq. per litre. He was excreting in his urine 0·5 mEq. of calcium and 0·2 mEq. magnesium per day. He was in a positive calcium balance (5 mEq. per 24 hours), and in a negative magnesium balance (5 mEq. per 24 hours).

Magnesium Repletion

After the convulsions, the patient was given magnesium 200 mEq. intravenously (100 mEq. over 4 hours on 2 consecutive days). The plasma-magnesium level reached 3·7 mEq. per litre at the end of the second infusion. The urinary magnesium and calcium increased to 53 and 12 mEq. per 24 hours respectively. The patient retained about 80 mEq. of the injected magnesium.

During the next 4 days magnesium (50 mEq. per day) was given by mouth. The plasma-magnesium dropped to 1·2 mEq. per litre, and the urinary magnesium to 5 mEq. per 24 hours, but the urinary calcium excretion remained unchanged.

During the next 4 days, the oral magnesium intake was increased to 200 mEq. daily, and supplemented with 10 mEq. given by intramuscular injection. Calciferol therapy was discontinued. On this regime the plasma-magnesium rose to 1·6 mEq. per litre. The urinary magnesium and calcium also rose to 20 and 40 mEq. per 24 hours respectively.

* To enhance the accuracy of estimation of the fæcal output, chromium sesquioxide was given to the patient in doses of 0·5 g. t.d.s. (Whitby and Lang 1960). This substance is not absorbed from the gut, and thus the daily fæcal loss of any substance may be calculated by determining its ratio to chromium in a sample of fæces.

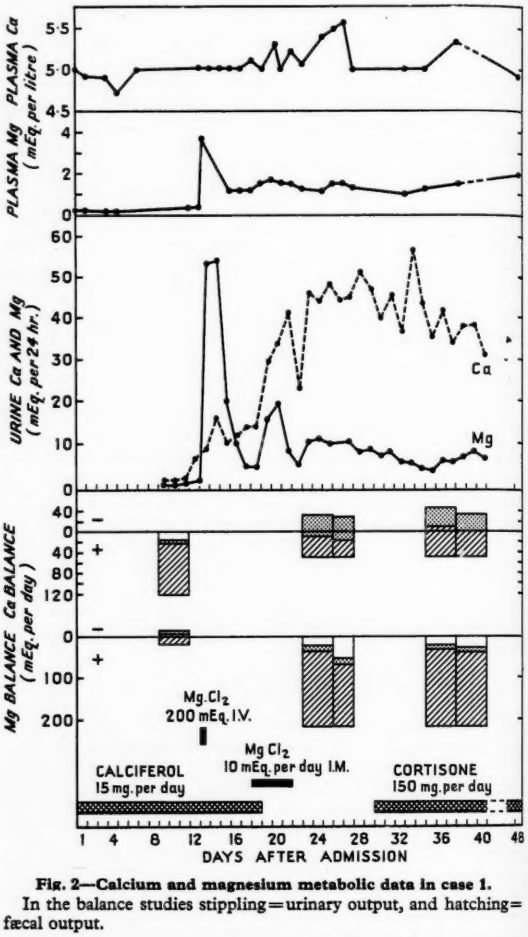
PLASMA Ca (mEq. per litre)
PLASMA Mg (mEq. per litre)
URINE Ca AND Mg (mEq. per 24 hr.)
Ca
Mg
Mg BALANCE Ca BALANCE (mEq. per day)
Mg.Cl2 200 mEq. I.V.
Mg Cl2 10 mEq. per day I.M.
CALCIFEROL 15 mg. per day
CORTISONE 150 mg. per day
DAYS AFTER ADMISSION

Fig. 2—Calcium and magnesium metabolic data in case 1.
In the balance studies stippling = urinary output, and hatching = fæcal output.

When the intramuscular magnesium supplements were stopped, the urinary magnesium and calcium dropped to 5 and 22 mEq. per 24 hours respectively for a day, and then returned to 10 and 50 mEq. per 24 hours. The plasma-magnesium fell gradually over 3 days to 1·2 mEq. per litre, and then it fluctuated, reaching 2 mEq. per litre on discharge.

Cortisone Therapy

When cortisone (150 mg. per 24 hours was added to this regime the fæcal calcium increased slightly from 30 to 45 mEq. per 24 hours, but the serum and urinary levels did not change.

Throughout the period of large oral magnesium supplements, the patient showed not only a positive magnesium balance (average 25 mEq. per 24 hours) but also a negative calcium balance (average 25 mEq. per 24 hours). The latter was largely due to high urinary calcium loss, the fæcal calcium being about equal to the intake.

Discussion

The syndrome of magnesium deficiency has been well studied in animals. Kruse et al. (1932) showed that when rats are given a low-magnesium diet they develop dilatation of cutaneous blood-vessels, hyper-irritability, tachycardia, and generalised convulsions, which are frequently fatal. Nephrocalcinosis affects the proximal tubules (Hess et al. 1959), and is accompanied by hypercalcæmia (MacIntyre and Davidsson 1958). In other species magnesium deficiency produces similar convulsions—for example in rabbits (Kunkel and Pearson 1948), dogs (Orent et al. 1932), and calves

(Blaxter et al. 1954). This state in animals is often called tetany, but the seizures differs from those associated with calcium deficiency both in their nature and in their response to drugs (Greenberg and Tufts 1938).

In man, on the other hand, the syndrome of magnesium deficiency is much less clearly defined. Tetany, tremors, choreiform movement, fibrillary twitches, delirium, rigidity, confusion, status epilepticus, cerebellar symptoms, stupor, and athetoid movements have all been reported in association with hypomagnesæmia (Miller 1944, Flink et al. 1954, Harmon 1956, Potts and Roberts 1958, Randall et al. 1959). But Martin et al. (1952), in a study of 16 patients with plasma-magnesium levels less than 1 mEq. per litre, did not elicit any symptom or sign clearly due to hypomagnesæmia. They emphasised the absence of tetany.

Confusion has arisen from the use of the term tetany by several workers to describe the syndrome of experimental magnesium deficiency; despite their use of this term they clearly recognised the syndrome as distinct from hypocalcæmic tetany. The differences were emphasised by Greenberg and Tufts (1938) although they also used "tetany" to describe the syndrome. The misnomer led to a search for hypomagnesæmia in patients with tetany and neuromuscular disturbances. Since most of these patients had multiple electrolyte and nutritional disturbances (Randall et al. 1959), it is hardly surprising that a low plasma-magnesium was sometimes found.

In the cases reported here, certain features appeared to be due purely to magnesium deficiency. These were: (1) a positive Chvostek sign without a concomitant Trousseau sign; (2) a low-voltage E.C.G.; (3) epileptiform convulsions and E.E.G. changes suggesting a focal cerebral lesion; and (4) possibly depression and irritability, ataxia, and muscular weakness. All these features were rapidly restored to normal by correction of the magnesium deficiency. In case 1 the diarrhœa was more severe in the absence of dietary magnesium supplements, both initially and later when the magnesium mixture was temporarily withheld. The very low plasma-alkaline-phosphatase level, which rapidly rose when magnesium was given, suggests a causal relationship, and recalls the similar observations of Snyder and Tweedy (1942) in rats. None of the first patient's typical features of tetany was present when his serum-calcium level was corrected by oral calciferol. Tetany does not seem to be produced by magnesium deficiency.

In the first case several factors probably contributed to the magnesium deficit. Firstly, intestinal absorption of magnesium was impaired both by steatorrhœa, and also by the high-calcium intake. It has been shown in animals (Alcock and MacIntyre 1960) that magnesium absorption from the gut varies inversely with the calcium intake, and it seems possible that these two elements are absorbed by a common transport system. Thus excessive intake of either element would inhibit absorption of the other. This would be consistent with the negative magnesium and positive calcium balance which the first patient showed initially and which may have contributed to the hypomagnesæmia in the second case. Secondly, excessive renal loss of magnesium may have played a significant part. When the plasma-magnesium levels were restored, renal leakage of calcium and magnesium seemed to occur in the first patient. We suggest that this is best explained by postulating damage to a common renal tubular reabsorptive system for calcium and magnesium. Such a view gains some support from the work of Berglund and Forster (1958), who demonstrated a common transport system for divalent cations in the aglomerular teleost. A similar conclusion was drawn by Alcock and MacIntyre (1960) from experiments on the excretion of calcium in magnesium-deficient rats. In the second case magnesium deficiency was probably due to increased bone avidity for this element as a result of the removal of the adenoma.

Summary

Clinical and metabolic observations are recorded in three cases which showed hypomagnesæmia without other electrolyte deficiencies.

The clinical picture was very different from that usually ascribed to hypomagnesæmia. Tetany in the sense of spontaneous muscle-cramps was completely absent. The syndrome comprised: (1) a positive Chvostek's sign, with a negative Trousseau's signs; (2) a low-voltage electrocardiogram; (3) liability to epileptiform convulsions; and (4) depression, vertigo, ataxia, and muscular weakness.

All these signs and symptoms remitted rapidly when the serum-magnesium levels were restored to normal.

Addendum

Recent claims have been made by Vallee et al (1960) that hypomagnesæmia in man may cause tetany which is indistinguishable from that due to hypocalcæmia. But their conclusions are based on analytical results which seem open to question: not only does their normal range for serum-calcium differ considerably from widely accepted values (Schales 1953, King and Wootton 1956) but their normal range for serum-magnesium seems to be erroneously high by almost 20% (Alcock et al. 1960).

Further, these workers are mistaken in believing that magnesium deficiency in animals causes a state which is indistinguishable from hypocalcæmic tetany. Greenberg and Tufts (1938) recognised the clear clinical differences; they also showed that while neuromuscular disturbances in hypocalcæmia arise from the neuromuscular junction and can be inhibited by tubocurarine, the convulsions of magnesium deficiency arising from the midbrain are increased by tubocurarine. In cattle, the distinction is difficult because hypocalcæmia accompanies the hypomagnesæmia in 75% of cases (Allcroft 1954).

In the five cases reported by Vallee et al., one (case 5) had serum-magnesium levels well within their normal range. Of the other four cases, three are described as having convulsions and tetany (cases 1, 3, and 4). Case 2 had a low serum-calcium judged even by their normal range. In each of these cases the serum-calcium was low, and, although some of the symptoms may have been due to hypomagnesæmia, it seems more reasonable to attribute the tetany to the hypocalcæmia. In our experience, hypomagnesæmia alone does not cause tetany.

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References continued overleaf

EFFECT OF FOOD, ALCOHOL, AND HYOSCINE ON BODY-TEMPERATURE AND REFLEX RESPONSES OF MEN IMMERSED IN COLD WATER

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ALCOHOL, which has been known for many years to cause vasodilatation (Cushny 1910), tends (Gaddum 1949, Harrison 1952) to accelerate the falls in temperature of men exposed to cold. The present experiments were designed to show if it did this to an important extent in men immersed in cold water. The effect of hyoscine was also studied since it is a common seasickness remedy and may have been taken by victims of shipwrecks.

The effect of a heavy meal was also investigated on account of the popular belief that it is dangerous to swim after a heavy meal. Sudden death in cold water is generally ascribed (Simpson 1958) to vagal arrest of the heart following inhalation of water into the nose and glottis; but alternatively (Keatinge 1959) it might be caused by ventricular fibrillation due to the increase in intravascular pressure (Bondurant et al. 1957, Keatinge and McCance 1957), hyperventilation, and release of adrenaline caused by sudden exposure to cold. Ventricular extrasystoles are common when men are suddenly immersed up to the neck in cold water (Keatinge 1960). Electrocardiographs were therefore taken and the degree of hyperventilation assessed in the present experiments to find out whether food, alcohol, or hyoscine affected them.

Methods

The subjects were ten healthy Naval ratings aged 18–28. Each was immersed up to the neck in stirred water at 15°C for 30 minutes, every 2nd day for 8 days, wearing only cotton trunks, a helmet, and a mask. The immersions were made in an indoor tank equipped with a powerful mechanical stirrer (Keatinge 1959), and during them the men sat still in it on a slatted wooden seat. The water was kept at 15±0·1°C by refrigerating equipment; the temperature of the immersed skin has been shown to fall to within 1° of 15°C within 2 minutes of such an immersion (Keatinge 1959).

The men's rectal temperatures were measured by a thermojunction enclosed in semirigid plastic tubing and inserted 11 cm. from the anus; the cold junction was in a vacuum flask of ice and water and the E.M.F. led to a potentiometer. Readings were accurate to the nearest 0·05°C. The air expired during immersions was passed through a Kofranyi-Michaelis gas meter and sampler; the oxygen deficit of the sample was measured by a Hartmann and Braun analyser; and the mean metabolic rates were calculated by the method of Weir (1949). The oxygen deficit of the expired air was used as an indication of the men's degree of hyperventilation. The cardiac record was made from waterproof leads on the men's wrists for 60 seconds before immersion and from the 15th to the 70th second after they entered the water. The men's heart-rates were counted from the last 10 seconds of each record. Peripheral blood-flow was estimated by a heat-flow disc (Hatfield 1949) stuck on the dorsum of the terminal phalanx of the right index finger and supported by a rubber band; the finger was always dipped into the tank for 10 minutes before the individual was immersed, to permit an estimate to be made of blood-flow in the finger while the body was still warm.

All the immersions were made in the afternoon between 2.30 and 4 P.M., and each man was always immersed at the same time of day. Before each immersion the men spent 30 minutes in the tank room, which was kept at 24–27°C by thermostatically controlled electric heating. 45 minutes before immersion they either drank 75 ml. absolute alcohol (diluted with 125 ml. water), or swallowed a tablet of hyoscine hydrobromide (gr. $^1/_{100}$), or ate a heavy meal (tomato soup, $^1/_2$–1 lb. sausages with bacon and tomatoes, about $^1/_2$ lb. bread with butter and jam, about $^3/_4$ lb. of apple pie, and 1–2 glasses of orange squash). Before another (control) immersion, they took nothing. Before the experiments the men always spent the morning quietly in a warm room, and ate a normal lunch at noon. The order in which subjects 1–4 and 7–10 went through the experiments was crossed-over in two latin-square patterns; but subjects 5 and 6 went through their four experiments in opposite orders, thus making a straight cross-over rather than a complete latin-square for these two men.

Statistical comparisons were made on a paired basis, the data in any type of experiment being compared to the individual data obtained in the "control" immersion. Data were all assumed to be normally distributed except for heat-loss from the finger; these often contained values much higher than the mean and were therefore subjected to non-parametric analysis by the sign test.

Results

Table I shows that just before immersion the men's rectal temperatures were, on average, somewhat lower after alcohol and higher after hyoscine than before the control immersion, while their finger heat-losses were usually somewhat higher after alcohol and lower after hyoscine. After a heavy meal their rectal temperatures and peripheral blood-flows were both rather higher than before the control immersion. These differences, however, were all small and not significant, and the men's heart-rates and skin temperatures were very similar before each of the immersions.

TABLE I—RECTAL TEMPERATURES, SKIN TEMPERATURES, HEART-RATES AND FINGER BLOOD-FLOWS (MEANS AND RANGES) BEFORE IMMERSION

—	Food or drug before immersion			
	None	Heavy meal	Alcohol	Hyoscine
Rectal temperatures (°C)	37·65 (37·35–37·85)	37·76 (37·45–38·05)	37·57 (37·15–37·90)	37·75 (37·35–37·95)
Skin temperatures (°C)	34·30 (33·31–35·33)	34·44 (33·05–35·53)	34·04 (33·35–35·38)	34·52 (33·55–35·75)
Heart-rates (beats/min.)	82·3 (64·8–98·9)	85·7 (72·7–102·0)	84·0 (69·0–102·6)	79·0 (64·6–86·5)
Blood-flow in index finger (cal./sq. cm./min.)	0·043 (0·021–0·131)	0·064 (0·004–0·193)	0·074 (0·028–0·131)	0·035 (0·021–0·056)

Table II shows that, although the rectal temperatures of most men fell somewhat faster after a heavy meal and after alcohol than in the control immersion, the difference was small and was not significant in either case. Hyoscine had no effect. The table also shows that the rectal temperature of each man fell at a rate which differed greatly from man to man but was fairly constant for each individual.

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Table III shows that, although the men maintained during immersion a significantly higher loss of heat from the finger when they had taken alcohol than when they had not, their digital blood-flows even after alcohol were very low within 8 minutes of immersion; neither food nor hyoscine affected them.

Table IV shows that alcohol usually reduced the metabolic rate, often substantially. It failed to do so, however, in three men, all of whom were singing and moving about during the immersion. Hyoscine reduced the metabolic rate in every man except one; this effect was significant at the 0·01 level.

Table V shows that alcohol reduced, and hyoscine abolished, the rise in the men's heart-rates on immersion and that the latter effect was highly significant. It also shows that some men developed ventricular extrasystoles on immersion, and that these were somewhat more frequent after a heavy meal or hyoscine than in the control immersion, while there were none after alcohol. Hyoscine significantly increased the men's hyperventilation as assessed by their expired-air oxygen deficits, in the first 10 minutes of immersion, while alcohol had no effect on them.

TABLE II—FALL IN RECTAL TEMPERATURE (°C) DURING IMMERSION

Subject no.	Food or drug before immersion			
	None	Heavy meal	Alcohol	Hyoscine
1	0·05	0·40	0·10	0·10
2	0·65	0·80	0·80	0·90
3	0·25	0·80	0·50	0·45
4	1·10	1·35	1·45	1·35
5	0·80	1·30	0·90	0·80
6	0·80	0·60	0·35	0·40
7	2·20	2·75	2·30	2·30
8	1·50	0·85	1·85	1·50
9	0·35	0·50	0·35	0·10
10	0·80	0·75	1·00	0·50
Mean	0·85	1·01	0·96	0·84

Subjective Effects

After alcohol the men seemed quite comfortable in the water and after leaving it said that it had felt much less cold than in other immersions; many described it as quite warm. A heavy meal produced no clear subjective effects in the water, and hyoscine none except dryness of the mouth. Minor cramps in the leg muscles were common in the thinner men towards the end of immersions, but the only severe one was in subject 4's "hyoscine" immersion.

Discussion

It has frequently been stated that alcohol should not be taken by men before exposure to cold, on the grounds that it is a vasodilator drug and will accelerate their falls in temperature (Gaddum 1949, Harrison 1952). In cold water, however, it did not do so significantly, even in quite large doses, and finger heat-losses always declined rapidly to low levels when the men were immersed in water at 15°C. Although the men's finger heat-losses fell distinctly less rapidly after alcohol than without it, the vasoconstriction induced by the cold was clearly sufficient to overcome very largely the vasodilator effect of the alcohol. In experiments on prisoners (Alexander 1946) alcohol was reported to accelerate the fall in temperature in cold water, but the total number of subjects was small and the average fall was little greater in the men who had taken alcohol. In the present experiments there were large and fairly consistent individual differences in the rate at which different men's temperatures fell; these had been observed previously on the same men (Keatinge 1960) and shown to depend mainly on the thickness of the subcutaneous fat.

TABLE III—RATE OF HEAT-LOSS FROM THE INDEX FINGER (CAL./SQ. CM./MIN.) 8 MIN. AFTER IMMERSION

Subject no.	Food or drug before immersion			
	None	Heavy meal	Alcohol	Hyoscine
1	0·000	0·002	0·002	0·004
2	0·000	0·004	0·002	0·000
3	0·000	0·002	0·002	0·002
4	0·000	0·000	0·002	0·002
5	0·000	0·000	0·004	0·000
6	0·005	0·002	0·012	0·002
7	0·000	0·002	0·002	0·000
8	0·004	0·004	0·005	0·005
9	0·005	0·012	0·039	0·004
10	0·004	0·007	0·005	0·002
Mean	0·002	0·003	0·008	0·002
			Differs from col. 1 $P<0·01$	

TABLE IV—METABOLIC RATES DURING IMMERSION (K.CAL./MIN.)

Subject no.	Food or drug before immersion			
	None	Heavy meal	Alcohol	Hyoscine
1	1·99	2·48	1·81	1·96
2	1·59	1·80	1·50	1·25
3	3·13	2·77	3·75	2·86
4	6·29	6·53	4·27	6·33
5	3·25	3·50	3·34	2·58
6	2·16	3·02	2·02	2·07
7	4·90	4·65	3·99	4·06
8	5·12	4·77	5·13	4·20
9	3·02	4·51	2·49	2·95
10	2·84	2·88	2·28	2·28
Mean	3·43	3·69	3·06	3·05
				Differs from col. 1 Sd 0·111 $P<0·01$

TABLE V—CHANGE IN HEART-RATE, VENTRICULAR EXTRASYSTOLES, AND OXYGEN DEFICIT OF EXPIRED AIR DURING IMMERSION

—	Food or drug before immersion			
	None	Heavy meal	Alcohol	Hyoscine
Change in heart-rate in 1st min.:				
Mean	+6·2	+7·8	+2·1	−0·6
Range	−7·9– +30·4	−10·3– +23·7	−14·5– +29·1	−18·5– +20·5
				Differs from col. 1 Sd 1·37 $P<0·001$
Ventricular extrasystoles 15–70 sec. after immersion:				
Total no.	2	7	0	5
No. of men who developed them	1	3	0	3
Oxygen deficit of air expired in 1st 10 min. of immersion:				
Mean	2·99	3·17	3·04	2·72
Range	2·53– 3·50	2·30– 3·53	2·00– 4·07	1·97– 3·53
				Differs from col. 1 Sd 0·103 $P<0·05$

Hyoscine is known to cause hyperventilation (Wangeman and Hawk 1942) and did so in the present experiments, although it decreased the men's metabolic rates and eliminated their rise in heart-rate in the water. The hyperventilation and consequent alkalosis will presumably increase the risk of cramp in the water, and the only man to get severe cramp in these immersions had it after hyoscine.

The numbers of ventricular extrasystoles were not large enough to assess with any confidence the effects on them of food, alcohol, and hyoscine. Their greater frequency after food suggests that the popular belief in the danger of swimming after a meal may be justified, although the risk cannot be great. Their absence after alcohol suggests that alcohol reduces any such risk, presumably by reducing the intensity of the initial vaso-

constriction. Their greater frequency after hyoscine may be a result of hyperventilation produced by this drug; a sudden large fall in the plasma-pCO_2 of dogs can cause ventricular fibrillation (Brown and Miller 1952). The present experiments therefore show that alcohol is unlikely to accelerate greatly the falls in temperature of people who abandon ship into cold water, and that it may possibly reduce the risk of sudden immersion and will certainly reduce the discomfort. Gross drunkenness could clearly be hazardous, but there seems little reason why people forced to enter cold water after shipwreck should forego the subjective relief that moderate amounts of alcohol can provide, and the subjective relief may itself have a survival value by reducing the risk of panic. It is interesting that after the sinking of the *Titanic* the only man who survived immersion in the water until the arrival of the rescue ship is said (Lord 1956) to have had a considerable amount of alcohol.

Summary

Neither 75 ml. of alcohol, nor a heavy meal, nor gr. $^1/_{100}$ hyoscine taken 45 minutes before immersion significantly affected the rate at which men's rectal temperatures fell during 30 minutes' immersion in water at 15°C; blood-flows in their fingers always fell rapidly to low levels in the water although they fell significantly less rapidly after alcohol.

Several men developed ventricular extrasystoles on immersion; most of these were observed after hyoscine or a heavy meal, and no extrasystoles were observed after alcohol.

Alcohol greatly reduced the men's discomfort and sensation of cold in the water.

Alcohol usually reduced the men's metabolic rates and the increase in their heart-rates during immersion; hyoscine reduced their metabolic rates and abolished the increase in their heart-rates, but unlike alcohol did not affect their subjective sensation of cold.

We are indebted to Prof. R. A. McCance for his support and interest, to Surgeon Captain F. E. Ellis for making the Naval volunteers available, to Dr. H. Lawn for operating the electrocardiograph, and to the subjects for their cooperation.

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"... the most significant circumstance is that the attitude of the world at large probably did not seriously determine the course of science. In the 17th century the contest was largely a battle of the books. The opponents of the Royal Society did little effectively to hinder it. Nor indeed, after the first flush of enthusiasm did the majority of its non-scientific or fashionable supporters do very much actively to help it. The records of sermons, pamphlets and other forms of the written word is the raw material of a one-sided story. The literary basis of so much history can easily falsify the perspective. Writers express their views and other writers, by the natural working of affinity, often attach undue importance to the evidence that these afford. A few dramatists can characterise a whole period as licentious, even resolutions of undergraduate debating societies if they catch the fancy of the journalists may help to fix a label on an age. But the future germinates unknown and silently."—Sir CYRIL HINSHELWOOD, P.R.S., Tercentenary Address of the Royal Society, Royal Albert Hall, London, July 19, 1960.

BLOOD PYRUVATE AND LACTATE RESPONSE OF NORMAL SUBJECTS TO DEXTROSE, SUCROSE, AND LIQUID GLUCOSE

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IT is well established that metabolites such as pyruvate and lactate attain higher levels in the blood after the administration of fructose than after dextrose (Root et al. 1946, Miller et al. 1952, Smith et al. 1953). It has been suggested that this reflects differences in the metabolism of the two sugars.

Since sucrose given by mouth is hydrolysed to dextrose and fructose before absorption it was thought that studies on the pyruvate and lactate response to this sugar would be of interest. In this paper the results obtained after the administration of sucrose to ten normal subjects are presented and the findings compared with those observed after similar doses of dextrose and liquid glucose. Liquid glucose is a complex carbohydrate substance produced by the hydrolysis of starch. According to data published by the technical advisory bureau, Corn Industries Research Foundation (1956) it was calculated to contain approximately (% w/w) dextrose 14·8, disaccharides (mainly maltose), 11·0, higher oligosaccharides (tri-hepta saccharides) 33·2, dextrins (octa and higher saccharides) 19·4. On complete hydrolysis to monosaccharides liquid glucose yields dextrose only.

TABLE I—PYRUVATE AND LACTATE LEVELS IN TEN SUBJECTS GIVEN DEXTROSE, SUCROSE, AND LIQUID GLUCOSE

Subject	Sugar given	Blood-pyruvate (mg. per 100 ml.)			Blood-lactate (mg. per 100 ml.)		
		Fasting	60 min.	90 min.	Fasting	60 min.	90 min.
C. O.	D	1·18	1·08	1·00	7·6	9·1	8·1
	S	0·80	1·20	1·16	5·8	13·9	8·3
	LG	0·45	0·61	0·65	5·6	7·3	7·1
M. A.	D	1·11	1·15	1·11	7·0	7·5	8·0
	S	0·88	1·24	1·32	7·8	12·0	13·1
	LG	0·65	0·54	0·62	3·9	4·2	8·0
S. A.	D	0·89	1·11	1·08	5·9	9·4	9·8
	S	0·92	1·72	1·48	6·4	17·6	18·0
	LG	0·81	0·89	0·65	6·4	8·6	7·5
M. O.	D	0·65	0·73	0·58	4·4	10·2	10·7
	S	0·65	1·75	1·59	3·9	19·9	18·8
	LG	0·82	0·86	1·02	3·3	7·5	7·3
E. P.	D	1·00	1·00	0·92	4·7	5·9	7·4
	S	0·61	1·47	1·59	5·1	10·7	13·0
	LG	0·73	0·69	0·90	3·3	7·7	7·5
M. T.	D	0·47	0·39	0·47	5·8	8·6	6·5
	S	0·20	1·35	1·10	3·7	13·5	15·4
	LG	0·34	0·72	0·72	4·4	5·7	5·2
B. U.	D	0·68	0·68	0·70	4·2	5·0	4·9
	S	0·31	0·72	0·53	6·7	10·5	6·1
	LG	0·56	0·56	0·54	4·0	4·7	6·8
R. I.	D	1·19	1·20	1·23	4·9	10·9	8·6
	S	1·03	1·75	1·54	3·3	13·2	12·3
	LG	1·10	1·04	1·04	3·4	8·0	5·4
G. A.	D	0·46	0·84	1·02	5·0	5·8	7·0
	S	0·53	1·67	1·96	5·6	8·3	7·7
	LG	1·04	1·46	1·24	5·7	6·5	7·8
G. L.	D	0·31	0·27	0·24	5·1	7·9	7·2
	S	0·20	0·74	0·57	2·1	11·2	8·5
	LG	0·51	0·61	0·41	4·6	5·7	6·5

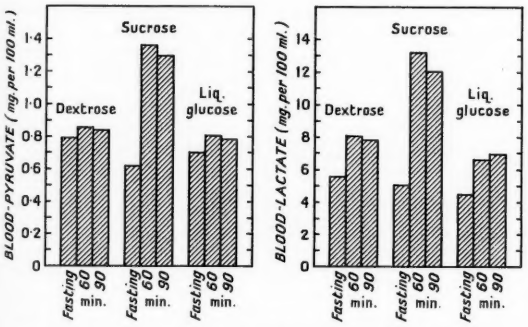
D=dextrose. S=sucrose. LG=liquid glucose.

Method

The subjects were all healthy young medical students, seven male and three female (E. P., M. A., and R. I.).

Standard pyruvate-tolerance tests using the technique described by Williams et al. (1943) were carried out after administration of the three carbohydrates.

The subjects fasted overnight. On arrival for the test they rested on a couch for half an hour, after which a fasting blood sample was taken. They then drank a solution equivalent to 45·4 g. of the sugar to be investigated dissolved in 250 ml. of water (i.e., 45·4 g. sucrose, 50 g. dextrose monohydrate, or 56·8 g. liquid glucose). A further similar dose was given thirty minutes later. Further blood samples were collected 60 minutes and 90 minutes after the fasting sample. All blood samples were obtained by venepuncture without stasis. The blood was collected into bottles containing a mixture of cetyl triethylammonium bromide, sodium fluoride, and a citrate buffer as an anticoagulant-preservative, and prepared as



Mean blood-pyruvate and blood-lactate levels in the subjects.

described by Long (1946). Each subject attended three times, receiving a different sugar on each occasion; the order in which the sugars were administered to the different subjects was not, however, the same.

The initial period of rest was necessary because preliminary control experiments showed that even mild activity could produce fluctuations in the fasting pyruvate level comparable with the response seen after dextrose. They also showed the fasting pyruvate level to fall during the first hour of complete rest.

Pyruvate determinations were carried out by the method of Friedman and Haugen (1943) and the lactate determinations by the method of Barker and Summerson (1941).

Results

The results obtained are shown in table I and the responses to the three sugars compared in the accompanying figure which shows the mean values for the ten subjects. The rises in pyruvate and lactate after the administration of dextrose and liquid glucose are comparable. After sucrose higher levels are attained in every subject. The mean 60-minute values for both pyruvate and lactate are more than double the mean fasting level, whereas the rise following the other two sugars is less than +20% for pyruvate and +50% for lactate. The relevant figures are compared in table II.

After 90 minutes, the pyruvate has returned to normal in six subjects after the administration of dextrose and in five subjects after liquid glucose, but it remains above the fasting level in every subject after sucrose. The 90-minute lactate levels tend to remain raised above the fasting level after all three sugars, but whereas after dextrose and liquid glucose the mean rise persisting is less than 2·5 mg. per 100 ml., after sucrose the mean

TABLE II—MEAN 60-MINUTE RISES ABOVE FASTING LEVEL DERIVED FROM TEN SUBJECTS

—	Pyruvate (mg. per 100 ml.)	Lactate (mg. per 100 ml.)
Dextrose	0·06 (*7·6%*)	2·5 (*45·5%*)
Sucrose	0·75 (*123%*)	8·1 (*162%*)
Liquid glucose ..	0·11 (*15·9%*)	2·1 (*46·6%*)

90-minute value is 7·1 mg. per 100 ml. above the fasting level.

Discussion

Reference has already been made to the fact that fructose produces higher levels of pyruvate and lactate than dextrose. We have confirmed this observation (unpublished data). In pyruvate-tolerance tests in three subjects, the mean 90-minute pyruvate level after fructose was 2·03 mg. per 100 ml. whereas after dextrose it was only 0·69 mg. per 100 ml.

It seems likely that the difference in level of carbohydrate metabolites produced by dextrose and sucrose is due to the metabolism of the fructose moiety of the sucrose molecule. It is, in fact, difficult to suggest any alternative hypothesis.

The liver is quantitatively the most important site of fructose metabolism. It is doubtful whether brain can utilise fructose to any great extent under physiological conditions, since Bollman and Mann (1931) showed that in the eviscerated dog blood-fructose levels of 100 mg. per 100 ml. failed to prevent hypoglycæmic convulsions when the blood-glucose fell below a critical level. Chain (1959) has compared the metabolism of dextrose and fructose by rat-brain slices and finds that the formation of aminoacids from fructose is only about one-third of that from dextrose; the formation of lactate only about one-fifth; and the production of CO_2 only about one-half.

Utilisation of fructose by muscle in vivo is slow or possibly negligible. Wick et al. (1953) working with eviscerated, nephrectomised rabbits and administering ^{14}C-labelled fructose showed that the fructose was distributed in a volume equivalent to that of the extracellular fluid and that very little fructose entered the intracellular fluid even after 6 hours. Insulin did not speed the transfer as it does with dextrose. They also showed that the rate of formation of $^{14}CO_2$ from ^{14}C-labelled fructose was less than 5% of that from ^{14}C-dextrose. They conclude that there is little extrahepatic utilisation of fructose.

There is evidence, therefore, that if the higher levels of pyruvate and lactate after sucrose are due to metabolism of the fructose moiety, this metabolism of fructose is occurring in the liver. Why higher levels of pyruvate and lactate should occur after fructose than after dextrose has been discussed by a number of workers without any wholly satisfactory conclusion being reached (Root et al. 1946, Miller et al. 1952, Smith et al. 1953). There is little doubt, however, that this finding reflects the different metabolic pathways followed by these two sugars in the liver.

Fructose is converted by a specific fructokinase, which has no action on glucose, to fructose 1-phosphate. This is split by an aldolase to two three carbon fragments, D-glyceraldehyde and dihydroxyacetone phosphate. The D-glyceraldehyde may be phosphorylated to give glyceraldehyde-3-phosphate. Dihydroxy-acetone phosphate may also be readily converted to glyceraldehyde-3-phosphate by triose phosphate isomerase. Condensation of two molecules of triose phosphate will give rise to fructose-1-6-diphosphate which may be used for the synthesis of

glycogen. Alternatively D-glyceraldehyde phosphate derived from both these carbon fragments may be further metabolised via phosphoglyceric acid to pyruvate and so enter the tricarboxyllic acid cycle.

Glucose, after phosphorylation by hexokinase to yield glucose-6-phosphate, can produce two molecules of triose phosphate by the reactions of the glycolytic pathway.

It has been suggested that the rate of conversion of glucose to glucose-6-phosphate by hexokinase may be a rate-limiting step in the metabolism of glucose (Krebs and Kornberg 1957, Beck 1958). If this is so, the existence of two separate enzymes for the phosphorylation of glucose and fructose and of two independent pathways for the formation of triose phosphates from these sugars may possibly account for the more rapid rise in blood-pyruvate and blood-lactate following sucrose feeding.

Furthermore, since fructose feeding produces only a slight rise (less than 20 mg. per 100 ml.) in the peripheral blood-fructose level in subjects with normal hepatic function it would seem that the fructokinase reaction is relatively rapid. Thus fructose may be more rapidly converted to triose phosphate and thus to pyruvate than glucose which is phosphorylated initially by the slower hexokinase reaction, so that production of pyruvate from fructose is more rapid than its utilisation by way of the tricarboxyllic acid cycle. This would account for the higher levels of pyruvate and lactate which occur in peripheral blood. This is supported by evidence that in rat liver phosphorylation of fructose by A.T.P. occurs at a greater rate than that of glucose (Long 1952).

The accumulation after ingestion of sucrose of one of the most reactive key intermediates in carbohydrate metabolism, pyruvate, which forms the link between fat, aminoacid, and carbohydrate metabolism is an interesting fact which not only indicates that sucrose and dextrose are utilised in different ways, but also that the effects of these sugars on fat and aminoacid metabolism may be different and warrant further investigation.

Summary

(1) Pyruvate and lactate responses to dextrose, sucrose, and liquid glucose have been studied in ten normal subjects, fasting and at rest, using the classical pyruvate-tolerance test technique.

(2) The responses to dextrose and liquid glucose were similar.

(3) The rise in both pyruvate and lactate levels in the blood was greater after sucrose than after either dextrose or liquid glucose in every subject.

(4) The higher levels of metabolites seen after sucrose are probably the result of hepatic metabolism of fructose derived from the sucrose molecule.

We would like to thank the students who undertook the tests, and Miss Margaret Hobart and Mr. H. G. Stevens who carried out the analyses.

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ANTENATAL DETERMINATION OF FŒTAL SEX IN PREVENTION OF HEREDITARY DISEASES

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AT the end of 1955, within a period of five weeks, four groups of investigators submitted papers to various journals on antenatal determination of the fœtal sex (Fuchs and Riis 1956, Shettles 1956, Serr et al. 1955, Makowski et al. 1956). The methods, developed independently in Copenhagen, New York, Jerusalem, and Minneapolis, were identical, and confirmation of the results was soon obtained (James 1956, Dewhurst 1956, Keymer et al. 1957, Pasquinucci 1957). Thus, the problem of the diagnosis of fœtal sex which had "always challenged attention, intrigued interest and baffled solution" (Blakely 1937) was no longer a problem.

The simultaneous development of the method in different parts of the world was no wonder. Barr and his coworkers' discovery of sex chromatin in intermitotic nuclei from female cells (Moore et al. 1953) formed the basis, and the finding that sex chromatin could be demonstrated not only in living tissue but also in desquamated cells from mucous membranes (Marberger et al. 1955, Moore and Barr 1955) was the immediate cause of the thought that cells in the amniotic fluid might show the sex of the fœtus.

Although the diagnosis of the fœtal sex can be made from the end of the first trimester, the procedure should not be carried out to satisfy the curiosity of the parents, since it requires puncture of both the uterus and the membranes. And as a matter of fact, in spite of public interest in the method, we have not had a single request for the procedure out of curiosity.

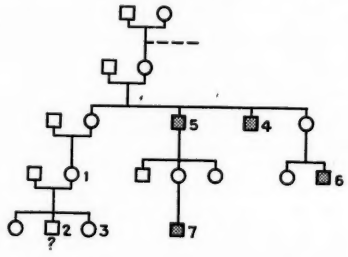
It was thought, however, that this method and the method developed later for determination of the fœtal blood-group before birth (Fuchs et al. 1956a) could be useful in prevention of hereditary diseases (Edwards 1956, Sachs and Danon 1956, Fuchs et al. 1956b). We have now had opportunity to make use of antenatal sex determination in two mothers who were hæmophilia conductors.

According to the Danish Act of 1956 concerning interruption of pregnancy, legal abortion may be granted "if there is close risk that the child, due to inherited characteristics or to disturbance or disease acquired during fœtal life, may come to suffer from mental disease or deficiency, epilepsy, or severe and non-curable abnormality or physical disease". A woman wishing to have her pregnancy interrupted under this and other legal clauses must apply to the Mothers' Aid Institution. The case will then be studied from medical and social aspects, and when this special clause is applicable the Institute of Human Genetics in the University of Copenhagen is asked to make a statement concerning the risks for the fœtus. The final decision is made by a board consisting of a psychiatrist, a gynæcologist, and a social worker. In

the cases to be described the Institute of Genetics found strong evidence that the two mothers were conductors of hæmophilia with 25% risk of giving birth to boys with hæmophilia. Permission for abortion was granted in both cases.

Case-histories

Case 1.—The first patient was 27 years old and of Dutch origin but married to a Dane. Her pedigree is shown in the accompanying figure. The patient is 1, and 2 and 3 are her second and third children. Her grandmother had four sisters and five brothers who were all said to be well. Her maternal uncles are 4 and 5: the first died aged 19 of a hæmoptysis



Pedigree for case 1. The hatched squares indicate known cases of hæmophilia. The numbers are referred to in the text.

(he had pulmonary tuberculosis); the other is alive, 50 years old, with hæmophilia, and the son of his daughter also has hæmophilia (7). The same applies to 6, a cousin of the patient (Prof. S. van Crefeld in Amsterdam has kindly confirmed the diagnosis in this case).

Our patient has hyperextensible fingers and maintains that even small lesions cause prolonged bleeding. Her first pregnancy in 1951 ended with the birth of a living girl, weighing 2000 g. (4·4 lb.). In 1954 she became pregnant again, but this time she requested and was granted a legal interruption of pregnancy on eugenic grounds. Her third pregnancy was in 1957, and this time she decided to carry it through. She went into labour about two months before term and was delivered of a premature boy as a breech. The boy, weighing 1350 g., was in poor condition and died five hours later. Unfortunately, his blood was not examined. The blood loss at delivery was 600 ml., and there was an impression in the placenta corresponding to one cotyledon.

One of us saw her for the first time on this occasion and advised her to get in touch with us if she became pregnant. This she did in January, 1959, and she now maintained that she would not continue her pregnancy if there was a risk of bearing a boy with hæmophilia. The eugenic indication for interruption of pregnancy remained unchanged and was confirmed by the local board of the Mothers' Aid Institution. We then suggested trying to determine the sex of the fœtus, and the patient was ready to have the procedure carried out and wished to continue her pregnancy, if the fœtus was found to be female.

The patient was admitted to the gynæcological department of Kommunehospitalet, and two days before and two days after the procedure she was given 100 mg. progesterone in oil intramuscularly daily. For the puncture of the uterus the patient was given a sedative but no anæsthesia. A long thin needle was inserted through the uterine wall from the anterior fornix. 12 ml. of clear yellow amniotic fluid was withdrawn and replaced by a similar quantity of 0·9% saline.

The amniotic fluid was centrifuged and the sediment was stained for sex chromatin. The cells were typical amniotic fluid cells, and the majority were chromatin-positive.

The patient was informed that the test indicated the presence of a female fœtus. She agreed to continue her pregnancy and was discharged with no sign of imminent abortion.

The pregnancy continued without incident until the end of the seventh month, when she began to bleed intermittently from the vagina. She was admitted to the obstetrical department A of Rigshospitalet, Copenhagen, and during the next sixteen days she bled at intervals of a few days. The presence of a total or partial placenta prævia could be excluded. After slight pains for two nights she went into labour and rather suddenly delivered a live girl weighing 1150 g. (2·53 lb.). The baby was resuscitated with oxygen and placed in an incubator. After four weeks she was transferred to a pædiatric hospital, and at three months old she was discharged in good condition.

Bleeding-time and coagulation-time of the patient before delivery was $3^1/_4$ and $2^1/_2$ minutes respectively, by the simple clinical tests. An examination of a blood sample at the Statens Seruminstitut revealed, however, that addition of anti-hæmophilia substance B to the blood much improved coagulation.

The fact that the patient was delivered prematurely in every non-interrupted pregnancy makes a relation between the puncture of the ovum in the fourth month and the antepartum hæmorrhage and the premature delivery unlikely, although it can by no means be excluded.

Case 2.—This patient was 21 years old and engaged to be married. A year before she had had an illegal abortion. The present pregnancy was desired, but in the middle of the fourth month she was told she was a conductor of hæmophilia. Her physician referred her to the Mothers' Aid Institution, after receiving confirmation of the diagnosis from the Institute of Human Genetics, because of her fear of giving birth to a boy with hæmophilia. Three brothers of her mother have hæmophilia, a sister of her maternal grandmother has a son with the disease, and other cases are known in the family (Sjølin 1960). The coagulation-time (Andreassen 1943) was $9–12^1/_2$ minutes, and this was considered to demonstrate the presence of the hæmophilia gene in the patient.

The patient agreed to have the amniotic fluid examined for the sex of the fœtus, while the board of the Mothers' Aid Institution ruled that interruption of pregnancy would be granted if the fœtus was masculine, and added that interruption would have been granted without conditions if the test had not been possible.

The patient was admitted to the gynæcological department and treated in the same way as case 1. Puncture from the vaginal fornix was unsuccessful, however, because only blood was aspirated in two attempts. Two days later puncture was carried out through the abdominal wall without difficulty, and 12 ml. of clear, yellow amniotic fluid was replaced by the same quantity of saline. The fluid contained chromatin-positive cells. Informed that the fœtus was probably female, the patient, now in the 17th week of pregnancy, left the hospital without signs of imminent abortion.

Nearly four months later she was admitted to the obstetrical department A of Rigshospitalet because she had felt no fœtal life for about two weeks. No heart-sound could be heard, but X-ray examination showed no definite signs of fœtal death. Two days after the examination she went into labour and delivered a dead girl, weighing 2450 g. (5·39 lb.), greatly macerated, and with the cord once around the neck. There were no visible malformations. The placenta had to be removed manually in pieces; it was inserted on the anterior side of the uterus.

Discussion

Puncture of the uterus and the ovum from the vagina, and even through the abdominal wall, in the fourth month of pregnancy, carries very limited risks to the mother (Alvarez and Caldeyro Barcia 1950). Perforation of the bladder can be avoided by emptying it beforehand; it is rarely harmful, but if urine is mistaken for amniotic fluid, the cytological examination will always show chromatin-positive cells. Perforation of the intestines is

unlikely from below and can be avoided in puncture through the abdominal wall by careful palpation. Infection of the uterine contents is probably the most important risk, but it should be small if the sterile technique is efficient.

The risks to the fœtus are undoubtedly greater. Infection of the ovum and lesions of the placenta, the cord, or the fœtus may cause abortion. In a small series of cases, in which interruption of pregnancy was carried out several days after aspiration of amniotic fluid, none of this was observed (Juhl and Fuchs 1956). A small lesion might not give an immediate effect, however, but may cause fœtal death later. Trasler et al. (1956) reported abortions and congenital malformations of the fœtuses of mice, subjected to puncture of the ova through the uterine wall on the 13th day of gestation. The malformations consisted in cleft palates, and the reason was thought to be loss of amniotic fluid, restricting the embryo and pushing its head down on the chest and thereby forcing the lower jaw upwards. For this reason we replace the amniotic fluid with the same quantity of saline. Leakage of fluid into the vagina has not been observed in our cases.

We are unable to explain the fœtal death in case 2 nearly four months after the puncture. But since the puncture is carried out only to save the fœtus in half of a number of cases, otherwise to be aborted, a certain risk to the fœtus should probably not prevent the procedure. We feel it justified to continue in order to evaluate the risks, because the method seems to be useful in preventive eugenics. It is beyond the scope of this paper to discuss the justification of interrupting pregnancies in conductors of hæmophilia. It is worth remembering, however, that in spite of great advances in the knowledge of hæmophilia, the average life expectancy in the most recently published material (Ikkala 1960) is 17 years.

Besides hæmophilia, certain other severe sex-linked recessive hereditary diseases are known, such as pseudoglioma with grave mental deficiency (Dahlberg-Parrow 1956). Moreover, the procedure is not restricted to determination of the fœtal sex. ABO blood-groups can be determined with the same accuracy, but to our knowledge no severe blood-group-linked hereditary disease is known at present. It is not unlikely that in the future it might be possible, by examination of the amniotic fluid or the cells in it, to diagnose before birth some of the metabolic enzyme defects now known to be the cause of severe disorders.

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NEEDLE BIOPSY OF THE LUNG

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IN a patient with chest-disease the diagnosis may remain doubtful despite careful clinical examination, sputum analyses, radiography, and bronchoscopy. Examination of sections of lung tissue may then prove invaluable. A lung-biopsy specimen may be taken at open operation or by needle puncture.

The first diagnostic puncture of the lung, reported by Leyden (1883), was used to obtain microorganisms from a pneumonic lung. Menetrier (1886) made a diagnosis of carcinoma of the lung by microscopic examination of aspirated lung tissue. Patella (1888), Talamon (1888), Tchistovitch (1904), and other early observers mention the use of diagnostic puncture of the lung, particularly for bacteriological purposes. Hellendall (1899) first established a histological diagnosis of a pulmonary tumour by lung puncture. Horder described the procedure in 1909, being unaware of previous reports. In 1917 Hirschfeld, and in 1918 Deelman, reported their experience of diagnosing malignant tumours by lung puncture and aspiration. Martin and Ellis (1930), Stewart (1930), Sharp (1931), Sappington and Favorite (1936), Lanari and Pavlovsky (1937), Craver and Binkley (1939), Gledhill et al. (1949), and Storey and Reynolds (1953) mentioned needle biopsy of the lung in the diagnosis of intrathoracic lesions, which were mainly neoplasms.

We here report the experience gained from 137 cases which underwent needle biopsy of the lung. The Vim-Silverman biopsy needle was used instead of the aspiration technique employed in all previous studies. These cases include all varieties of chest-disease, including tuberculosis and 1 case of cor pulmonale; in all previous reports the technique was confined to pulmonary neoplasms, where the purpose was histological study, or to pneumonia, for bacteriological study.

Technique

Selection and Preparation of the Patient

1. Patients with pleural effusion should have the fluid removed before biopsy.

2. The patient must be cooperative because, if he breathes while the needle is in the lung, a longitudinal rent may be produced.

3. Biopsy should not be performed unless adequate facilities for blood-transfusion are available.

4. A mild sedative, such as amylobarbitone sodium, is given half an hour before biopsy. As cooperation is necessary, stronger narcosis should not be used.

5. Radiography is essential beforehand to exclude pulsating shadows. Posteroanterior and lateral views are necessary to localise the exact site of the lesion. We found no need to use metal calipers, as advised by Craver and Binkley (1939), to determine the size and depth of the tumour.

Procedure

The intercostal space overlying the lesion is used for puncture—anteriorly, in the axilla, or posteriorly—as shown by

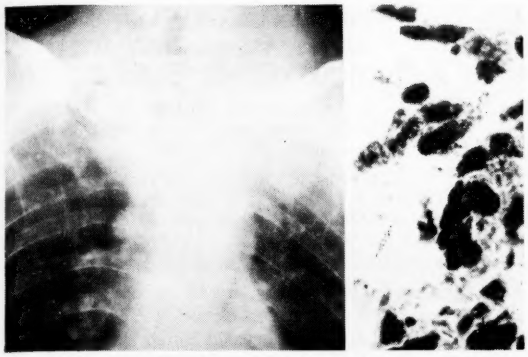

Fig. 1—Male, aged 42, with insidiously developing quadriplegia. Chest radiography showed that the trachea was compressed and displaced to the right by a large soft tissue mass causing bone destruction of the left borders of the upper three dorsal vertebræ and posterior parts of the left ribs. Needle biopsy of the mass revealed a bronchial adenocarcinoma, moderately well differentiated.

the radiographs. If there is clinical dullness, the site of maximal dullness is chosen.

The patient lies supine with the side on which the biopsy is to be done as near the edge of the bed as possible. A firm pillow is placed under that side to raise it, and to open the intercostal spaces, as for artificial pneumothorax. After preliminary cleansing, the skin is anæsthetised with procaine solution 2%. The skin need not be incised. A standard Vim-Silverman needle is inserted quickly, as for liver biopsy. The cylinder of lung tissue is then transferred to a bottle of fixative, and the puncture wound in the skin is sealed with simple collodion.

Aftercare

As a little local pain may follow the puncture a sedative, such as a mixture of chloral and potassium bromide, is given. The pulse is charted every two hours for the first day, and the physician should be called if the pulse-rate rises. It is advisable for the patient to stay in bed for twenty-four hours. The procedure causes very little discomfort, and those who have been subjected to artificial pneumothorax agree that biopsy is less unpleasant.

Indications for Needle Biopsy of the Lung

Diagnostic

Needle biopsy can be used when open thoracotomy is refused or is not feasible. We believe that the procedure should be used routinely in the diagnosis of chest-diseases, and should replace diagnostic thoracotomy. Needle biopsy is much easier than bronchoscopy, and less expensive than tomography, which exposes the patient and the radiographer to a huge dose of radiation; moreover needle biopsy may give much more definite results.

Table I shows the pathological diagnoses in the 137 cases in which this procedure was used. Figs. 1 and 2 illustrate the value of needle biopsy in diagnosis. Needle

TABLE I—PATHOLOGICAL DIAGNOSIS IN 137 CASES SUBJECTED TO NEEDLE BIOPSY OF THE LUNG

Diagnosis	No. of cases
Bronchogenic carcinoma	113
Tuberculosis	7
Mammary carcinoma	3
Non-specific pneumonitis	3
Sarcoidosis	2
Osteogenic sarcoma	2
Chondrosarcoma	1
Hodgkin's granuloma	1
Pulmonary schistosomiasis	1
Scleroderma	1
Pulmonary fibrosis secondary to infarct	1
Postirradiation pulmonary fibrosis	2

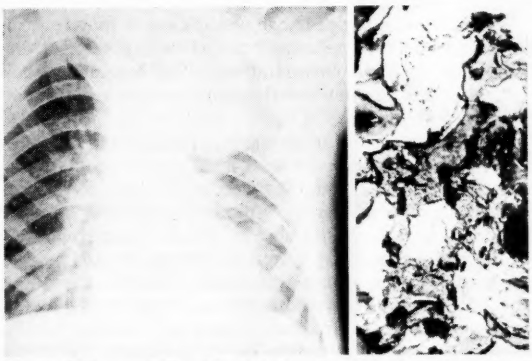

Fig. 2—Male, aged 58, with clinical and radiological diagnosis of left bronchogenic carcinoma, but negative bronchoscopy, proved by needle biopsy to be osteogenic sarcoma.

biopsy is also valuable in the pathological typing of bronchogenic carcinoma, which helps in deciding the treatment to be adopted. In our series the 113 cases of carcinoma were:

Anaplastic	52 (*46%*)
Squamous-cell	50 (*44%*)
Adenocarcinoma	11 (*10%*)

We found needle biopsy of the lung the most helpful single investigation in the diagnosis of bronchogenic carcinoma (table II); and indeed it was more useful than all other investigations combined.

Research

Needle biopsy is valuable in assessing the various methods of treatment. The histological changes of pulmonary tuberculosis under different antituberculous drugs can be studied and correlated with changes in the clinical picture, radiographical findings, sputum, &c. The response of malignant disease to antimitotic drugs or to radiotherapy can be watched. Needle biopsy can also be used to study the pathology of lung-diseases that rarely come to necropsy—virus pneumonia for example—and the natural stages of diseases, of which the terminal phase only is known. Histochemical methods may be applied to the biopsy specimen to demonstrate the basic constituents of the cell, and to localise enzymes; tissue culture, respiration studies, and microchemical determinations can also be performed.

TABLE II—VALUE IN BRONCHOGENIC CARCINOMA OF DIAGNOSTIC PROCEDURES IN 117 CASES WITH SUGGESTIVE CLINICAL AND RADIOGRAPHICAL FINDINGS

Diagnostic procedure	No. of cases
Positive bronchoscopy:	
Tumour seen, biopsied with positive result	81
No tumour seen, blind biopsy proved positive	6
Sputum positive for cancer-cells	59
Cancer-cells in pleural fluid (of 25 cases with effusion)	12
Positive needle biopsy of lung	113

Of the other 4 cases, 3 proved by needle biopsy to have tuberculosis, and the fourth to have osteogenic sarcoma.

Risks and Complications

The contraindications to needle biopsy of the lung are:

Uncooperative patients—e.g., young children.
Pulmonary hypertension.
Pulmonary arteriovenous fistula.
Pulmonary cysts and bullæ.
Hæmorrhagic diathesis.
Lung abscess.
Empyema.

It has been suggested that needle biopsy may lead to infection, and that negative findings do not exclude the possibility of a malignant tumour. The latter may certainly be true. But in this series only 1 patient experienced severe complications (table III) and he had pulmonary schistosomiasis with pulmonary hypertension; immediately after biopsy he had a brisk hæmoptysis, coughing up about 150 ml. of blood. We later avoided needle biopsy in any case with pulmonary hypertension. 5 other patients had slight complications (table III) which cleared smoothly.

We had no mortality or residual morbidity among our patients, no important infections, pleural shock or mediastinal shifting, and no unusual pain or cough. In a previous series of 92 cases (Craver and Brinkley 1939), the complications of needle biopsy were also slight. If performed on carefully selected cases by one experienced in the technique, and if the Vim-Silverman needle (and not the aspiration technique) is used, we believe that the procedure carries negligible risks—even less than the risks of artificial pneumothorax.

TABLE III—COMPLICATIONS OF 137 NEEDLE BIOPSIES OF LUNG

Complications	No. of biopsies
None	131 (95·5%)
Slight:	
Pleurisy	1 (0·75%)
Surgical emphysema	1 (0·75%)
Local pain	3 (2·25%)
Definite:	
Severe hæmoptysis	1 (0·75%)

Conclusions

The best treatment for intrathoracic lesions cannot be given without accurate histological diagnosis. The necessity for early diagnosis of unilateral solid pulmonary infiltrates suspected of being bronchogenic carcinomata is of the utmost importance. Bronchoscopy does not detect peripheral tumours, and even some central tumours. In such cases needle biopsy of the lung may be preferable to biopsy at open thoracotomy.

The technique of needle biopsy is simple and safe, and it usually gives sufficient material for an accurate diagnosis to be made.

In carefully selected cases and in experienced hands needle biopsy of the lung can be used as a routine means of diagnosing pulmonary lesions, together with radiography, sputum examination, and bronchoscopy.

Thanks are due to Dr. John Glen, senior chest physician at Springfield Hospital, Grimsby, for his kind help and advice.

Addendum

A further 27 patients have now been subjected to needle biopsy of the lung, and in 1 case this was complicated by pneumothorax. This woman, aged 79, had multiple shadows over both lung fields, and the diagnosis proved to be sarcoidosis.

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PRIMARY AMENTIA AND MICRO-ORCHIDISM ASSOCIATED WITH AN XXXY SEX-CHROMOSOME CONSTITUTION

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A NUCLEAR-SEXING survey among mentally defective patients in a State training school (Ferguson-Smith, Handmaker, and Hill) has revealed 2 male patients (out of 916) with a double complement of sex chromatin in somatic nuclei. This finding suggests that these patients have a more complex sex-chromosome constitution than, for example, the chromatin-positive cases of Klinefelter's syndrome which have a single sex-chromatin mass and an XXY sex-chromosome constitution (Jacobs and Strong 1959). A similar observation has been made recently in a *female* patient with ovarian dysgenesis, and apparently average intelligence, who was shown to have an XXX sex chromosome constitution (Jacobs et al. 1959). It appears that this particular nuclear sex anomaly may not be very rare among mentally retarded individuals, for both male and female patients have been found in at least two mental-deficiency hospitals (Barr et al. 1959, Ferguson-Smith, Handmaker, and Hill).

We report here the clinical findings and chromosome analyses of these two patients with primary amentia, micro-orchidism, and two sex-chromatin bodies in intermitotic nuclei.

Case-histories

THE FIRST CASE

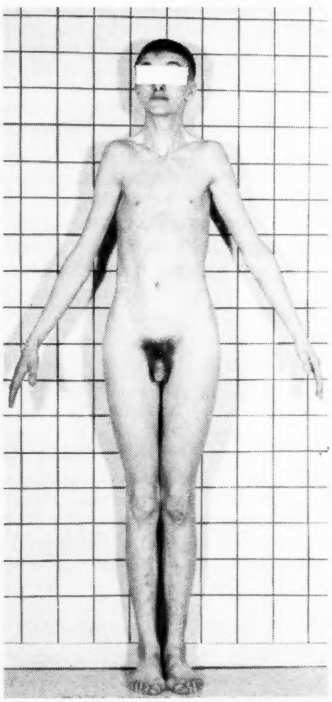

Fig. 1—First patient, aged 22.

The patient [J. H. H. no. 877961] is 22 years of age and of Polish-Austrian ancestry. Two brothers and seven sisters are healthy and all have children except the eldest brother, who is single. One sister has a male child (chromatin-negative) with hydrocephalus and multiple skeletal anomalies. At birth the patient was normal, but thereafter his rate of physical and mental development was retarded. Therefore at the age of 9 he was admitted to Rosewood State Training School. He is a placid, easily managed boy, who does simple work in the laundry. He does not shave, has had no acne, and is stated to lack libido.

He is a thin, asthenic male with a small head (51·5 cm. diameter) and disproportionately long legs (fig. 1). The chest is thin. He has round shoulders, lumbar lordosis, and webbing of the neck. There is bilateral radio-ulnar synostosis. The teeth are small, irregular, and partially erupted. The eyes are markedly myopic (−20D.) and the voice is in the high range for the normal male. The penis and scrotum show normal adolescent development. Very small firm testes are palpable bilaterally. The prostate is small. Pubic hair is profuse, but facial, axillary, and abdominal hair is scant, and there is no recession of the hair at the temples. Gynæcomastia is not present.

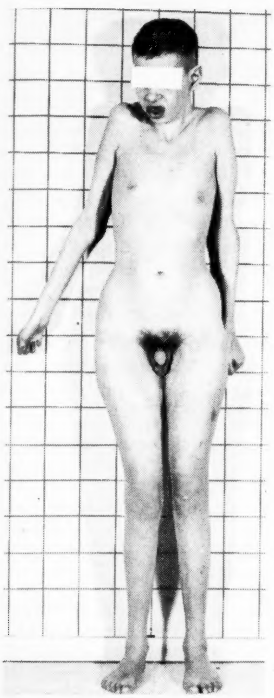

Fig. 2—Second patient, aged 22.

THE SECOND CASE

This patient [J. H. H. no. 178523] is also 22; his ancestry is Polish-Russian-Austrian. He has one sister, who is healthy and unmarried. The family history on the maternal side is noncontributory, but on the paternal side there is a strong history of schizophrenia, involving the father, uncle, grandmother, and cousin. At an early age he was noted to be very retarded and was admitted to Rosewood at the age of 9 with an estimated intelligence quotient below 20. He is unable to dress, feed, or care for himself, and his vocabulary is limited to a few simple words. Though of an anxious and nervous nature, he responds to simple directions and is generally cheerful and affectionate to those who look after him. He appears much younger than his stated age (fig. 2) and, like the first patient shows a low upper segment/lower-segment ratio. The pelvis is broad with android proportions, and there is no webbing of the neck. There is bilateral gynæcomastia, and the breasts have large areolæ with well-formed nipples. The larynx is normally developed. Facial hair is scant and there is slight temporal recession. Axillary and pubic hair are present, but chest and abdominal hair are absent. There is no acne. The penis and scrotum are adolescent. The testes are very small and are felt with difficulty high up in the scrotum. The prostate is palpable but small.

Tables I and II give further clinical data as well as the the results of special investigations.

The Investigations

The Testicular Lesion

At exposure for biopsy, the testes in both patients measured about 18 mm. in greatest length and appeared identical. The vas deferens and epididymis were normally developed on both sides without evidence of abnormal development of mullerian derivatives.

The histological appearance of the testis is very similar in the two cases. Apart from the presence of two sex-chromatin bodies in a large proportion of nuclei, it is that already reported in chromatin-positive Klinefelter's syndrome (Ferguson-Smith et al. 1957). Almost all the seminiferous tubules are completely atrophic and are represented by small hyalinised basement membranes which contain no elastic fibres. These "ghost" tubules blend into an amorphous connective-tissue stroma in which large islands of abnormal and pigmented Leydig cells are present. A few small seminiferous tubules, some partially hyalinised, are lined by Sertoli cells but contain no germinal cells. Hyalinisation is also apparent in some of the smaller arterioles in case 2.

TABLE II—SPECIAL INVESTIGATIONS

Case	Nuclear sex			Urinary excretion in 24 hours		Testis length at biopsy (mm.)
	Double sex chromatin	Single sex chromatin	Drumstick polymorphs	F.S.H. mouse units	17-ketosteroid (mg.)	
1	42%	38%	6/433	>52	4·2	18
2	36%	35%	6/725	<96	14·83	18

F.S.H. = follicle-stimulating hormone.

Chromosome Analysis *

Squash preparations were made from short-term bone-marrow cultures, and suitable mitotic cells were analysed as described previously (Ferguson-Smith, Johnston, and Weinberg 1960). In both cases the basic somatic number is 48 (see table III). Analysis of fifteen especially suitable cells in case 1 and five cells in case 2 clearly demonstrates the presence of a Y chromosome, and 15 chromosomes in group III. Measurements of these group III chromosomes reveal that the largest chromosome, with a submedian to median placed centromere, is trisomic (fig. 3). These results indicate that the sex-chromosome constitution in both cases is XXXY, for in our experience the largest chromosome in group III is the X chromosome.

TABLE III—CHROMOSOME COUNTS IN BONE-MARROW CELLS

Case	No. of cells with chromosome count of:					Total cells counted
	45	46	47	48	49	
1	10	11	13	116	2	153
2	8	13	9	87	1	118

Nuclear-sex Findings

As indicated in table II, the percentage of chromatin-positive nuclei in the oral smears (fig. 4) is high. This was not reflected in the frequency of the "drumsticks" in the polymorphonuclear leucocytes, and no double drumsticks were found.

In the relatives available for buccal smear—who included both parents of case 2 and the mother of case 1—the nuclear sex was normal.

Discussion

The severity of the mental defect in these two patients, and the additional congenital malformations in case 1, suggest that the XXXY sex-chromosome constitution is associated with a greater disability than the XXY constitution in chromatin-positive Klinefelter's syndrome. However, sex differentiation is the same in these two sex-

* An addendum to the paper by Ferguson-Smith, Johnston, and Weinberg, published last week, explains the method of numbering the chromosomes.

TABLE I—CLINICAL DATA

Case	Age	Maternal age at birth	Paternal age at birth	Sibship position	I.Q. Wechsler full scale	Skeletal age	Height (cm.)	Span (cm.)	Lower segment (cm.)	Ratio of upper segment to lower segment
1	22	38	52	10/10	49	17	170·5	164	93	0·83*
2	22	27	31	1/2	<20	22	175·0	177	94	0·86*

*Average for normal white males aged 22 is about 0·92 (McKusick et al.).

Fig. 3—Chromosomes from a bone-marrow cell in first patient, arranged in pairs. 2n=48 (XXXY).

Fig. 4—Nucleus of an oral mucosal cell of first patient, showing two typical sex-chromatin masses. (Cresyl echt violet. ×1500.)

chromosome anomalies, indicating that the additional X has no influence in this regard. The testicular lesion is almost indistinguishable in the two conditions, and by this criterion the XXXY syndrome must be considered a fourth variant of the Klinefelter syndrome (Ferguson-Smith et al. 1960).

The type of sex-chromosome anomaly reported here is more complex, and accordingly more difficult to explain on present theories, than those previously described. The XO constitution in chromatin-negative gonadal aplasia (Ford et al. 1959), the XXY constitution in chromatin-positive Klinefelter's syndrome, and the XXX constitution in the double chromatin-positive patient with ovarian dysgenesis, may be satisfactorily explained by *non-disjunction* of the sex chromosomes at one cell division, either during meiosis in the parental germ-cells, or during the early divisions of the fertilised ovum. The various types of non-disjunction and the possible factors affecting the frequency of non-disjunction in these conditions are considered in detail in a recent review (Ferguson-Smith 1960). It is sufficient to say here that non-disjunction at *one* cell division cannot lead to a zygote with an XXXY complement. For this to occur by the mechanism of non-disjunction, there are several theoretical possibilities:

1. Primary meiotic non-disjunction of the sex chromosomes in both parents: fertilisation of an XX-bearing ovum by an XY-bearing sperm.
2. Primary meiotic non-disjunction at both the reductional and equational divisions in either parent: fertilisation of an XXX-bearing ovum by a Y sperm, or an X-bearing ovum by an XXY-bearing sperm.
3. Secondary meiotic non-disjunction in an XXX mother with or without primary meiotic non-disjunction in the father: fertilisation of an XXX- or an XX-bearing ovum by a Y- or an XY-bearing sperm.
4. Mitotic non-disjunction in an XXY zygote at the first cleavage division: development from the XXXY daughter cell and elimination of the XY daughter cell.

We have excluded secondary non-disjunction as a possible mechanism only in so far as the mothers have only a single complement of sex chromatin (and presumably have only two X chromosomes), and the father of case 2 is chromatin-negative. Secondary non-disjunction in the deceased father of case 1 is considered very unlikely, since none of the numerous reported cases of chromatin-positive Klinefelter's syndrome have shown enough spermatogenesis to be fertile. Conclusive evidence on secondary non-disjunction must await chromosome analyses of the parents.

The alternative mechanisms cannot be tested until we can mark the human X-chromosome with several sex-linked genes (such as colour-blindness) and so trace the fate of the individual X chromosomes in a given pedigree. Recently this method has been used successfully to demonstrate the origin of the XO exception in the house mouse (Russell et al. 1959).

The Origin of the Sex Chromatin

The finding of two sex-chromatin bodies in the nuclei of these patients, and the very convincing evidence that they have three X chromosomes raises a problem concerning the origin of the sex chromatin.

An early suggestion was that the sex chromatin is formed of heterochromatic parts of the two X chromosomes which remain paired in the intermitotic nucleus (see Barr 1959). On this hypothesis one might expect to find *four* and not three X chromosomes in cells which have two sex-chromatin bodies. An alternative explanation would be that the sex chromatin is derived from heterochromatic parts of one X chromosome. Observations on nuclear-sex dimorphism in some lower species—e.g., the domestic fowl (Kosin and Ishizahi 1959)—support this because the sex chromatin is found in the heterogametic and not the homogametic sex. In addition, Ohno et al. (1959) have found that at mitotic prophase in the female rat, one of the X chromosomes shows positive heteropyknosis compared with the other chromosomes, and this chromosome can be related morphologically to the sex chromatin in the intermitotic nucleus. The male rat lacks this specific chromocentre and does not show differential heteropyknosis of any of the prophase chromosomes.

This hypothesis for the origin of the human sex chromatin is attractive because it does not invoke somatic pairing of the chromosomes and could explain the findings in the sex-chromosome anomalies. If these studies on prophase cells could be confirmed in man, the number of sex-chromatin bodies could be related directly to the number of heterochromatic X chromosomes, and there would be very strong evidence for differential behaviour of the two X chromosomes. It is possible that the differentiation is induced by paternal transmission and lost during oogenesis.

The theoretical implications of this are far-reaching. As an example, in the present context, it suggests that, in the genesis of the XXXY individual, non-disjunction occurs during spermatogenesis at both meiotic divisions leading to formation of an XXY-bearing sperm which fertilises a normal X-bearing ovum; for, in order to have two sex-chromatin bodies the two heterochromatic X chromosomes must have been derived from the father.

Summary

Survey of a mental-deficiency hospital has revealed two male patients with a double complement of sex chromatin in intermitotic nuclei. Chromosome analysis indicates that they have a chromosome number of 48 and an XXXY sex-chromosome constitution.

The findings are discussed in regard to the origin of the sex-chromosome anomaly and the significance of nuclear sexing.

We gratefully acknowledge the cooperation of Dr. Harry G. Butler, clinical director, and the members of the medical and nursing staff of Rosewood State Training School, Maryland, U.S.A. We are grateful to Dr. Claude J. Migeon for the hormone assays (work supported by research grant A.180 from the National Institutes of Arthritis and Metabolic Diseases, U.S. Public Health Service), to Dr. W. N. Toole for performing the testicular biopsies, and to Ciba Pharmaceutical Products Inc. for a generous supply of ' Colcemide '.

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Preliminary Communication

EVIDENCE FOR GENETIC PREDISPOSITION TO FORMATION OF THYROID AUTOANTIBODIES

THYROID autoantibodies, which are usually present in the circulation of patients with Hashimoto's disease and non-goitrous myxœdema [1–3] are less often demonstrable in other thyroid disorders—e.g., thyrotoxicosis and non-toxic nodular goitre.[2] In addition, low-grade thyroid autoimmunity has been reported in 5–6% of hospital patients without overt thyroid disease.[2–4] Since thyroid disease generally is known to run in families,[5] and clinically different thyroid syndromes—e.g., myxœdema, thyrotoxicosis, and non-toxic goitre—may arise within the same family,[6 7] we have recently looked for circulating thyroid antibodies in the relatives of patients with autoimmune thyroid disease.

To date, we have had positive serological results in 22 of 39 siblings studied, only few of whom showed obvious thyroid dysfunction. Preliminary communication of this finding seems warranted by the prima-facie evidence it offers of a genetically determined predisposition to thyroid autoimmunity.

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2. Roitt, I. M., Doniach, D. *ibid.* 1958, p. 1027.
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TABLE I—THE PROPOSITI

Patient	Sex	Age (yr.)	Diagnosis	Antibody to thyroglobulin (units*)	Complement-fixing antibody†
M.P.	F	49	Non-toxic goitre	8	0
M.M.	F	35	Myxœdema	14	+++
H.L.	F	60	Thyroid lymphosarcoma‡	13	++
G.W.	M	45	Myxœdema	16	+
E.H.	F	63	Non-toxic goitre	10	0
E.H.	M	53	Thyrotoxicosis	16	++++
L.F.	F	52	Myxœdema	10	0
L.M.	F	15	Non-toxic goitre	5	+
F.L.	F	60	Myxœdema	12	+++
A.D.	F	53	Myxœdema	8	0
E.K.	F	58	Hashimoto's disease	8	+

*Determined by tanned-red-cell agglutination. Arbitrary units of concentration corresponding to number (n) of serial twofold dilutions of original 1 in 5 serum dilution. Reciprocal of titre: 5×2^n.
†Strength of complement-fixation reaction, from weak (+) to very strong (++++).
‡Presumed to have arisen on pre-existing Hashimoto's thyroiditis.

TABLE II—INCIDENCE OF THYROID AUTOIMMUNITY AMONG SIBLINGS OF THE PROPOSITI

—	No. of siblings examined	No. with antibody to thyroglobulin only	No. with complement-fixing antibody only	No. with both antibodies	Total
Females	29	7	0	11	18
Males	10	2	1	1	4
All siblings	39	9	1	12	22

MATERIAL AND METHODS

11 propositi formed the starting-point of the investigation, all being patients under the care of one of us (G.A.S.) for some form of thyroid disease, and all possessing circulating autoantibodies in appreciable concentration (table I). They were the first such patients encountered after we had decided to begin the study, and there was no other basis of selection.

Antibody to thyroglobulin was estimated by a previously described adaptation [8] of the tanned-red-cell agglutination method of Boyden.[8] Complement-fixation technique followed in essentials that employed by Roitt and Doniach.[2]

RESULTS

The propositi have 44 known siblings, of whom 39 have been examined. 22 (56%) proved to have thyroid autoantibody in the circulation. In 9 this was directed against thyroglobulin alone, in 1 against the complement-fixing or " microsomal " antigen alone, and in the remaining 12 both types of antibody were present (table II).

TABLE III—INCIDENCE OF THYROID AUTOIMMUNITY AMONG OTHER RELATIVES

Relationship	No. of relatives examined	No. with antibody to thyroglobulin only	No. with complement-fixing antibody only	No. with both antibodies	Total
Parents	2	1	0	0	1
Children	10	1	0	3	4
Aunts, uncles, nephews, nieces	12	0	2	0	2

11 of the 22 had no clinical evidence of thyroid disorder. The commonest abnormality in the others was a palpably enlarged gland (7 cases); 2 were myxœdematous, and 2 had previously undergone thyroidectomy for thyrotoxicosis.

These results strongly suggest a genetic predisposition to thyroid autoimmunity, the frequency of circulating antibodies among siblings being close to the theoretical expectation of 50% for dominant inheritance. Much fewer data are so far available for other relatives (table III). Thus the only 2 parents examined were those of the propositus L. M., aged fifteen, none of the other parents being alive. Nevertheless, the combined incidence among parents and children (who like siblings have half their genes in common with a given propositus) was 5 out of 12, supporting the hypothesis of dominant transmission. The finding of antibodies in 2 of 12 more distant relatives (having a quarter of their genes in common with the propositi) is also consistent. We are accumulating data from other families to obtain a larger series of such relatives. Table II shows that positive serological findings were commoner among female siblings than among males.

8. Boyden, S. V. *J. exp. Med.* 1951, **93**, 107.

The difference is not at present statistically significant ($\chi^2=0{\cdot}7$), but the possibility of partial sex limitation is under investigation.

It is still uncertain how and why thyroid autoimmunity arises, but myxœdema has long been known to be familial, both in successive generations,[9] and in members of the same generation.[10] Familial examples of frank Hashimoto's disease are rare but undoubtedly occur.[11] On this basis, a genetic predisposition has been suggested.[12 13] Our findings strongly support the suggestion, although they throw no light on the possible nature of the genetic abnormality. This may be a defect in the gland itself, allowing contact between the immunity mechanism and substances normally confined to intracellular or intrafollicular sites—for example, in the follicular basement membrane.[14] Or it may involve the thyroid only secondarily, as when there is excessive stimulation by pituitary thyrotrophic hormone.[2] At present such considerations must remain speculative, though the familial occurrence of an abnormal iodine-containing protein in the circulation has been reported.[15] Our results certainly suggest that environmental factors, such as virus infection, are either not implicated in the development of thyroid autoimmunity, or they operate only against a background of genetic susceptibility.

The significance of autoimmunity in the pathogenesis of thyroid disease is also uncertain. In this respect, the high proportion of relatives without clinical thyroid abnormality but with serum autoantibodies is interesting. We intend to follow these subjects for a long time to determine the frequency of subsequent clinical manifestations of thyroid disease.

SUMMARY

Circulating thyroid autoantibodies were demonstrated in 22 of 39 siblings of patients with autoimmune thyroid disease. 11 of the affected siblings showed no other evidence of thyroid disorder at the time of examination. These findings are consistent with the view that the predisposition to develop autoantibodies to thyroid is inherited as a dominant characteristic.

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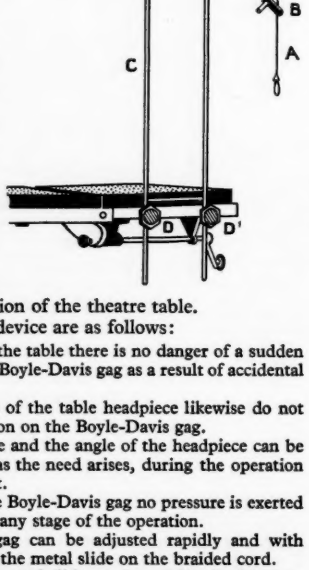
New Inventions

DEVICE FOR SUPPORTING BOYLE-DAVIS GAG DURING PHARYNGEAL OPERATIONS

THERE are innumerable contrivances in routine use for supporting the Boyle-Davis gag during tonsillectomy and other transoral pharyngeal operations, the variety of pattern reflecting the difficulty of achieving the ideal method of exerting the required traction. We have found at least one major objection to each of the many supports that we have used and have accordingly developed a new device (see figure) which we have found completely satisfactory.



The Boyle-Davis gag is supported by means of a piece of heavy braided cord (A), the length of which can be adjusted by moving a metal slide (B), attached to an S-hook. The cord is suspended from a metal stand (C), held by two running clamps of suitable design (D and D[1]) on the left-hand side of the head section of the theatre table.

The advantages of this device are as follows:

(1) Since it is attached to the table there is no danger of a sudden jerk being transmitted to the Boyle-Davis gag as a result of accidental movements of the table.

(2) Accidental movements of the table headpiece likewise do not produce changes in the tension on the Boyle-Davis gag.

(3) The height of the table and the angle of the headpiece can be adjusted from time to time, as the need arises, during the operation without releasing the support.

(4) Apart from that via the Boyle-Davis gag no pressure is exerted on *any* part of the patient at any stage of the operation.

(5) The tension on the gag can be adjusted rapidly and with delicate precision by moving the metal slide on the braided cord.

(6) The braided cord and metal slide can be sterilised with ease; hence the surgeon can make fine adjustments in the tension on the gag during the operation.

(7) The tension exerted is at the optimal angle for extending the neck, to give the best possible airway, without producing hyperextension.

(8) The stand does not obstruct the surgeon, the anæsthetist, or the theatre sister.

(9) The stand is conveniently portable and can be fitted to any standard theatre table; it eliminates the necessity of damaging the theatre walls by attaching wall supports and enables any theatre to be used for pharyngeal operations with the table in any desired position.

(10) It is stable, sturdy, and inexpensive, and can be set up with the greatest of ease.

We are indebted to Mr. Alec Chapman, who has constructed the prototypes used in the development of our present model, which was made for us by Messrs. A. C. Daniels & Co. Ltd., 41, New Cavendish Street, London, W.1.

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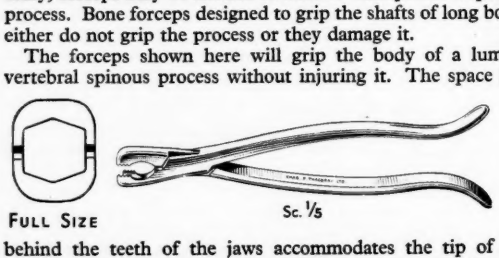
SPINOUS-PROCESS FORCEPS

DURING operations for the reduction of spinal dislocations, for spondylolisthesis, or for spinal fusion, or during laminectomy, forceps may be needed to hold or manipulate a spinous process. Bone forceps designed to grip the shafts of long bones either do not grip the process or they damage it.

The forceps shown here will grip the body of a lumbar vertebral spinous process without injuring it. The space just



behind the teeth of the jaws accommodates the tip of the process, which is thicker. The handles are long to allow for working at a depth, and they are curved to fit the grip of the whole hand.

The forceps are available from Messrs. Chas. F. Thackray, 10, Park Street, Leeds, 1.

The Royal Infirmary,
Sheffield, 6

W. J. W. SHARRARD
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Reviews of Books

The Clinical Application of Antibiotics

Vol. IV. Erythromycin and Other Antibiotics. M. E. FLOREY, M.D. London: Oxford University Press. 1960. Pp. 303. 84*s*.

THIS is the fourth and final volume of a detailed review of the clinical aspects of antibiotics, which began in 1952 with a first volume on penicillin; the second volume described streptomycin, the third chloramphenicol and the tetracyclines. The appearance of the fourth volume has been delayed, and it reviews the literature up to the end of 1957. Like its predecessors, it is a massive compilation of the published literature which will probably become the standard book of reference for many years. It is designed for the experienced clinician, or clinical teacher, who wishes to know on what authority the current views about antibiotics are based. The author quotes the leading clinical and laboratory publications on each subject and then gives a brief summary of the information. Thus the reader is given the average judgment, together with an indication of how widely individual opinions may range on each side.

The first two chapters describe erythromycin and the three related compounds, carbomycin, spiramycin, and oleandomycin. The next chapter discusses other antibiotics which control staphylococci and similar organisms, novobiocin, and vancomycin. Then four other antibiotics (framycetin, synnematin B, albomycin, and cycloserine) are reviewed. A fifth chapter deals with antibiotics whose use is limited by their toxicity, such as tyrothricin, bacitracin, and polymyxin; and a sixth chapter describes antibiotics active against protozoa, fungi, or neoplasms—e.g., fumagillin, nystatin, amphotericin (griseofulvin is not mentioned). The remaining third of the book is a chapter on the choice of antibiotic in special circumstances. This section takes note of new information which has accumulated since the publication of the previous volumes on penicillin, streptomycin, and the tetracyclines. In any serious disease it is necessary to consider the nature of the disease, the organism responsible, the sensitivity of the organism to the various antibiotics as shown by laboratory tests, and the previous history of the patient, who may show intolerance. Accordingly the correct choice may be a complicated procedure, and provisional treatment may have to be administered to control the infection while this information is being collected. The author emphasises that the value of antibiotic therapy is in a continual state of flux which may be altered at any time by the discovery of new antibiotics on the one hand or by the increased frequency of drug-resistant organisms on the other. In view of this danger of drug-resistance, the " routine use of antibiotics in hospitals, particularly as prophylactic measures, should be abandoned and their use limited to those cases where they are specifically indicated ".

The book is pleasing in binding and format; but it is a little difficult to consult and a few tables at the beginning or end, summarising indications and dosages, would have been welcome. Similarly the practitioner would welcome a list of the trade names to reveal the true identity of the many preparations pressed on his attention. The index is adequate; but, as this is apparently the final volume, a cumulative index would have rounded off the series.

The book is an invaluable work of reference, and Lady Florey is to be congratulated on having thus brought her masterly review of antibiotics and their clinical application to its full completion.

Leukaemia: Research and Clinical Practice

F. G. J. HAYHOE, M.D., M.R.C.P., lecturer in medicine, University of Cambridge. London: J. & A. Churchill. 1960. Pp. 335. 80*s*.

THIS book is a long and comprehensive review of the extraordinary amount of information that has accumulated about leukæmia. That so much of it is inconclusive is not Dr. Hayhoe's fault, but it does make the reader's task more irksome.

Beginning with a brief but interesting account of the historical development of knowledge about leukæmia, Dr. Hayhoe goes on to a classification that some may think has an old-fashioned look. Useful charts show the rising incidence of leukæmia, and the question of the influence of radiation is thoroughly examined; Dr. Hayhoe is unimpressed by the evidence that diagnostic X-rays have changed this incidence. Animal and especially murine leukæmias are discussed in detail, though the author thinks that " very few of these diseases appear to resemble the common leukæmias of man ". The chapter on the ætiology of leukæmia is comprehensive. There is a well-illustrated account of the application of histochemical methods, but no clear expression of opinion on their value; other methods of study are briefly cited. The many biochemical studies in leukæmia are described at some length, with much explanatory matter and appropriate diagrams, but the general inconclusiveness of most of these researches cannot be denied. The chapter on immunology includes a discussion of leucocyte antigens, and again the author notes that " experimental evidence is still lacking on too many fundamental issues for any firm conclusions to be drawn ". He reviews the now considerable work on in-vitro culture of leukæmic cells and notes that repeated experiments have confirmed the finding by the pioneers that there is no sharp or consistent difference in the behaviour in culture of normal and leukæmic leucocytes. From consideration of these experiments Dr. Hayhoe passes to the discussion of what is known of the action of X rays, antimetabolites, and antimitotic drugs on tissues; and this adds considerably to the bulk of the book. The available antimetabolites and cytotoxic agents, even those no longer or hardly ever used, are listed and their formulæ given.

The final third of the book is devoted to clinical aspects. The descriptions are very full, and every recorded symptom and sign is noted. Some illustrative but unremarkable case-records are provided. The cytological differentiation between acute myeloblastic, lymphatic, and monocytic leukæmias is given in tabular form with colour plates. Chronic myeloid and lymphatic leukæmias are dealt with in the same way. The chapter on unusual types of leukæmia is disappointing and unimpressively illustrated. The leukæmoid reactions are discussed at some length, and the book ends with two pages on the nature of leukæmia and its relation to neoplastic processes. The bibliography at the end of each chapter is very full.

Essays on the First Hundred Years of Anaesthesia

(Vol. I) W. STANLEY SYKES, M.B., D.A., late anæsthetist, General Infirmary at Leeds. Edinburgh: E. & S. Livingstone. 1960. Pp. 171. 30*s*.

THOUSANDS of volumes on medical history stand in our libraries; and if there is one aspect of the subject which has been more thoroughly considered than any other, it is the discovery of anæsthesia. It is hard to believe anything fresh could be written about it. Morton, running through the Boston streets clutching his glass globe, and late for his appointment with a tuberculous printer; Simpson, and Matthews Duncan, unconscious in an Edinburgh drawing-room; Wells, dead in a prison cell, his femoral artery opened by his own hand: these are dramatic figures certainly, but familiar ones. It is, therefore, a pity that there is nothing in the title of Dr. Sykes' book to indicate how different it is from anything which has preceded it.

After twenty-five years in practice as an anæsthetist, he has devoted his retirement to contemplating his professional predecessors and the equipment they used (he has descriptions or pictures of over 6000 different pieces of apparatus). This book contains his thoughts, often in a whimsical vein, on several matters which have often been taken for granted. One example is the story of John Snow and the Broad Street pump. This is generally recognised as being, to say the least, ill-founded. But how many know that there are reasons for doubting Liston's claim to have performed the first major operation under anæsthesia in Europe, and that he may have been anticipated, by two days, by a surgeon in Dumfries? Every

anæsthetic history describes how Victoria was given chloroform when Prince Leopold was born: what, then, is the significance of the authoritative denial, which appeared in *The Lancet*, five weeks after the Royal birth, that she had ever been rendered unconscious at all?

Any of the eight essays here presented could serve as a model of painstaking bibliographical research. The author's task has obviously been lightened by the incredible nature of several of the contrivances he encountered in his studies. His readers will share his enjoyment of such devices as Lawson Tait's anæsthetic apparatus and Leslie's resuscitation chair. In the former, ether in a glass vessel was heated over a naked flame: and the chair was designed to enable a moribund patient to breathe more deeply by moving his arms, which were fastened by rods to a treadle he was expected to work with his feet.

Studies on Vertebrate Neurogenesis

SANTIAGO RAMÓN Y CAJAL. Translated by LLOYD GUTH, M.D., National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda, Maryland. Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960. Pp. 432. 108*s*.

IN all branches of science certain figures stand out head and shoulders above their contemporaries. By the excellence of their work and the profundity of their thought these men lay lasting foundations which support all future work. Such a man was Santiago Ramón y Cajal. Spain has produced a number of artists but few scientists of the first order; in Cajal, however, she produced a genius whose scientific ability was linked with an intensely artistic nature. As a youngster he wanted to be an artist, drawing and painting with passionate enthusiasm, but his father, himself a physician, insisted that he should become a doctor. In this profession the young Cajal eventually found, after many vicissitudes, that anatomy and later histology gave full scope to both his scientific and artistic abilities. His interests became more and more centred on the study of histology, and many of his histological investigations were illustrated by his own drawings. He had been much fascinated by photography from the artistic viewpoint, and this interest helped him greatly in his studies of the nervous system, since the principles of the impregnation of nervous tissues with silver salts use the basic principles of the chemistry of photography. It was in the investigation of the histology of the nervous system that his genius reached its full development, and it was in this field that he made so many of the observations which form the basis of our knowledge of the structure of the nervous system. No-one can read his *Recollections of My Life* (published in translation in 1937 by the American Philosophical Society and now unhappily out of print) without gaining a unique insight into the development of neurological thought and a fascinating glimpse of the life of old Spain.

Cajal realised early that much vital information could be acquired by studying the nervous system of the embryo and the young animal, before the full complexity of the tissue had developed and this book comprises a series of his papers on the histology of the developing nervous system. Many of the papers were first published in journals which were obscure and are now defunct, and most of them were in Spanish and French.

The ground covered is extensive. There are papers on the development of motor, sensory, and sympathetic nerve-fibres and on their endings; on the origin of cells and nerve-fibres of the spinal cord. There is a considerable section on the cerebellum and the cerebral cortex, and the final part of the book is devoted to papers on the development of the cells of the retina.

The translation of these classical papers into English places them within easy reach of all who are interested in the nervous system. Zoologists, anatomists, neurologists, and neuropathologists alike will be indebted to the translator and publisher, who has made an excellent book, with good reproductions of the many illustrations.

This is a fundamental work which is bound to be referred to again and again by all workers on the nervous system and will find its place alongside Cajal's great text *Histologie du système nerveux de l'homme et des vertébrés*. The latter was recently reissued in French on the centenary of the author's birth, and it is to be hoped that a similarly public-spirited translator and publisher will one day put out an English translation of Cajal's greatest work. Then nearly all of his major work would be readily available to the English-reading world.

Neurology of Infancy

ANATOLE DEKABAN, M.D., PH.D., head, section on developmental neurology, National Institutes of Health, Bethesda. London: Baillière, Tindall, & Cox. 1960. Pp. 388. 96*s*.

THE author's object in writing is first to provide landmarks by which the normality or otherwise of development of the nervous system can be judged in the individual, and second to show how neurological disease differs in infants and in adults. The standards of normality are given in tables of anatomical detail, and in advice on examination of the physiological functions of the nervous system. Most of the book is devoted to descriptions of various neurological diseases in "infants", and is excellently illustrated with clinical and pathological photographs and with radiographs (which account for the rather high cost). In this country "infant" generally means a child under one year of age, but this book deals with the first few, especially the first two, years of life.

Atlas der Phasenkontrasthämatologie

HANSJÜRGEN RIND, DR. MED., assistant at the University Children's Clinic, Charité Hospital, Berlin. Berlin: Akademie. 1958. Pp. 392. 135*s*.

THIS is a good example of the volume traditionally associated with Teutonic learning. It is large, ponderous, and exhaustingly complete. There can be no corner of phase-contrast hæmatology that has escaped the author's attention. There are 1094 photographs of blood and bone-marrow cells, singly or in groups, taken by phase-contrast methods. Most of the photographs are 8 cm. by 6 cm.: six such photographs are arranged on a page and opposite there is a description, sometimes including an illustrative line diagram. The magnification favoured is 2000 times, and the photographic reproduction is superb; the clarity and sharpness of the detail is truly remarkable, and extreme care must have been taken in preparing the plates. The photographs naturally form the bulk of the book. There is a short preliminary section on theory, apparatus, and technique. After the photographs there are tables illustrating, by black-and-white diagrams, the characteristics of the different cell types, and lastly there is a list of references, citing mostly German papers and monographs.

Phase-contrast techniques are specially valuable when living unstained cells need to be studied at high magnifications. Such work is usually being carried out by experts who will not need an atlas to tell them what they are studying. For diagnostic hæmatology phase-contrast techniques have been a disappointment, and this atlas makes the disadvantages very clear. These photographs show the very best appearances that can be obtained; even so it is harder to differentiate the various cell-types than with the familiar stained smears illuminated by normal methods without any special and expensive optical apparatus. The larger libraries will no doubt have a copy of this atlas on the shelf for reference, but few individual workers need such an elaborate volume, however admirable.

Treatment of Cancer and Allied Diseases (2nd ed. *vol.* 3. London: Pitman Medical Publishing Co. 1959. Pp. 781. 231*s*.).—The third volume of the second edition of this considerable work, edited by Dr. G. T. Pack and Dr. I. M. Ariel, spares no expense in delivering the goods. The head and neck, excluding the brain, is covered in just over 700 pages profuse with illustrations. It is an undoubted work of reference which at 11 guineas not every library will be able to afford. There is a strong emphasis on the technical details of treatment both surgical and radiotherapeutic, and on the two combined, reflecting the practice of different centres all over the world.

THE LANCET

LONDON 23 JULY 1960

More Chromosome Anomalies

A YEAR or so ago, when three major human chromosome anomalies (XO Turner's, XXY Klinefelter's, and triple-21 mongolism) had been newly described within a very few months of each other, well-informed pessimists gave excellent reasons for supposing that the harvest remaining to be gathered in this field was small. Even if one considers only papers published recently in this journal on anomalies of the X chromosomes, it is evident that this prophecy was unjustified.

A disappointing but important negative finding may be mentioned first. Last week Dr. FERGUSON-SMITH and his colleagues [1] reported two cases, and Dr. DE ASSIS and his colleagues [2] another, of true hermaphroditism. Like most (but not all) such cases, these were chromatin-positive. All three had the normal total number of chromosomes (46) and the normal XX pair of sex chromosomes that might be expected from the sex-chromatin findings. These cases, together with two similar cases previously reported,[3 4] establish that a general anomaly of the chromosomes is not the cause of true hermaphroditism—or at least not the cause of the least rare form of this very rare disorder. The existence of true hermaphroditism is a stumbling-block to most theories of sexual differentiation. What endocrine pattern can explain, for instance, the simultaneous presence in one patient of active spermatogenesis in one gonad, ovulation in the other, and secretory endometrium in a rudimentary uterus? There has been no lack of attempts to explain this on chromosomal grounds. GRUNBACH and BARR [5] had an especially attractive idea involving incomplete sex reversal in a kind of *forme fruste* of Klinefelter's syndrome. This, and others, must go by the board. No general anomaly can account satisfactorily for a difference between the two sides of the body, and the only simple chromosomal origin for true hermaphroditism would be a mosaic in which part of the body was XX and part XY. Such mosaics may exist, but the mechanism of their production is hard to envisage. Moreover, there is no evidence from what little we know of chromosome mosaics in man (as distinct from insects) to suggest that they could have this kind of regional distribution. It is easy after the event to associate this particular line of investigation with woolly thinking; but it is the kind of woolly thinking which, allied to a new technique, has often paid dividends in the past. And it is by no means certain that all forms of hermaphroditism follow the pattern described.

Positive results are to be recorded in the form of at least four, and possibly five, anomalies of the X chromosomes. JACOBS et al. [6] described no less than three varieties. One of them was their second example of the XXX syndrome, rather inaptly named the "super-female". The patient who, unlike their original case, was mentally defective, had 47 chromosomes, trisomy of the X chromosome, and two sex-chromatin bodies in 48% of oral-mucosa nuclei. This syndrome, it begins to appear, is surpassed in frequency among recognised chromosomal anomalies only by mongolism and XXY Klinefelter's syndrome, and we should soon know a great deal more about it. The two other cases described by JACOBS et al. were examples of other and rather more bizarre anomalies: one case was in a woman with (apparently) loss of part of one X chromosome in all her cells, so that she deviated halfway towards an XO Turner's syndrome both clinically and in sex-chromatin content; the other was an especially remarkable case in a woman of whose cells half had only 45 chromosomes with an X missing (XO) and half had 47 chromosomes with an extra X (XXX). This case, in which the condition can hardly have arisen in any other way than by non-disjunction at the first cleavage of the fertilised egg (so that one of the two original cells contained an X too many, and the other contained one too few) is strong evidence for the view that mosaics in man are not likely to involve separate regions of the body; for—except for marrow, where conditions may be exceptional—the two races of cells were equally divided in the various regions examined.

The case reported last week by Dr. POLI and his colleagues [7] is claimed by them to be an example of a distinct syndrome, unrelated to X chromosome anomalies. Readers may wish to suspend judgment until the case is reported more fully. This "paramongol" seems to have been mongol-like only in obliquity of the palpebral fissures. The presence of two sex-chromatin bodies strongly suggest the XXX syndrome, though the percentage of affected nuclei is admittedly low. The patient has 47 chromosomes, and the extra chromosome is certainly not the small 21 of mongolism. It lies (to translate the notation used into the internationally agreed Denver system [8]) in the 6–12 group, which includes the X pair. POLI et al. believe that it is not an X but belongs to the 10th or 11th pairs. They may perhaps be in error, for distinction of the chromosomes in this group is extremely difficult. Alternatively the extra chromosome may be an abnormal X, with deletion of part of its longer arm—a combination in fact of the anomalies found separately in two cases by JACOBS et al.[6]

1. Ferguson-Smith, M. A., Johnston, A. W., Weinberg, A. N. *Lancet*, July 16, 1960, p. 126.
2. de Assis, L. M., Epps, D. R., Bottura, C. *ibid.* p. 129.
3. Harnden, D. G., Armstrong, C. N. *Brit. med. J.* 1959, ii, 1287.
4. Hungerford, D. A., Donnelly, A. J., Nowell, P. C., Beck, S. *Amer. J. hum. Genet.* 1959, **11**, 215.
5. Grunbach, M. M., Barr, M. L. *Rec. Progr. Horm. Res.* 1958, **14**, 255.
6. Jacobs, P. A., Harnden, D. G., Court Brown, W. M., Goldstein, J., Close, H. G., MacGregor, T. N., Maclean, N., Strong, J. A. *Lancet*, 1960, i, 1213.
7. de Carli, L., Nuzzo, F., Chiarelli, B., Poli, E. *ibid.* July 16, 1960, p. 130.
8. *ibid.* 1960, i, 1063.

Professor MURRAY BARR reported last year [9] the finding among both male and female mental defectives of cases with two sex-chromatin bodies in many nuclei. The females have already been explained as XXX. In an article which appears this week on p. 184, Dr. FERGUSON-SMITH and his colleagues report that such males are XXXY. As might almost have been deduced, the cases are essentially similar to the XXY Klinefelter's syndrome which FERGUSON-SMITH [10] earlier showed to be common among mental defectives—except that those with XXXY have a higher grade of mental defect and, in one case, some additional congenital defects. The origin of this latest anomaly is puzzling. Simple non-disjunction, which has explained so much, will not suffice: either some new kind of mechanism must be involved, or else there must have been two non-disjunctions. Improbable as it sounds at first, successive non-disjunctions, in both primary and secondary meiotic divisions, producing either an XXY spermatozoon or an XXX ovum, is the least unlikely of the hypotheses considered.

The fact that most of the anomalies discussed here are reflected in (and will usually be diagnosed by) abnormalities of the sex chromatin emphasises the importance of the relation of the sex chromatin to the X chromosomes. BARR's original hypothesis—that the sex chromatin represents the heterochromatin of the X chromosome pair—though it proved formidably productive, has suffered some attrition from the recent discoveries. In particular one would, as FERGUSON-SMITH says, expect a cell with two sex-chromatin bodies to have four X chromosomes, whereas it now appears to have three. And there are other difficulties, such as the absence of a half-sized body (derived from the single X) in males, and the absence also of sex chromatin from tetraploid male cells, which contain two Xs. OHNO's demonstration [11] that in the female rat only one chromosome (as seen in prophase) is heterochromatic has been widely accepted as evidence that the sex chromatin is derived from one X chromosome only. This idea, however, raises difficulties in its turn; for the heterochromatic chromosome clearly cannot be inherited as such (otherwise half of all males would have one such chromosome, and a quarter of all females two). OHNO's suggestion that the X chromosome inherited by a female from her father is heterochromatic (though not heterochromatic in the father) is ingenious but unlikely. Most of the facts (including the tetraploidy difficulty) could be explained by assuming that all X chromosomes are "naturally" heterochromatic, but that a single set of autosomes is sufficient to suppress heterochromaticity in one X. Thus, for example, an XXX cell has one set of autosomes, one suppressor, and so two heterochromatic Xs. But we hear rumours from the United States that chromatin-positive Turner's syndrome can be XO, and if this is so our hypothesis will be shortlived. This is tricky terrain, and the surprises it has to offer seem endless.

9. Barr, M. L., Shaver, E. L., Carr, D. H. *Proc. Canad. Fed. Biol. Soc.* 1959, **2**, 6.
10. Ferguson-Smith, M. A. *Lancet*, 1958, i, 928; *ibid.* 1959, i, 219.
11. Ohno, S., Kaplan, W. D., Kinosita, R. *Exp. Cell Res.* 1959, **18**, 415.

Thoughts on the Thyroid

FOR those interested in the thyroid, the past nine months has been a time of conferences and reviews. The season opened with a symposium on modern concepts of thyroid physiology, held by the New York Academy of Sciences in November, 1959, and subsequently published in the *Annals* [1] of that institution; and ended with the International Goitre Conference in London on July 5–8—the first to be held since 1938. Reviews have included an issue of the *British Medical Bulletin* [2] devoted entirely to the thyroid. Those concerned with this subject have therefore had plenty of opportunity for assessing progress.

The importance of techniques in determining the direction of advance is as evident here as in other branches of medical science: the investigator can do only what his tools permit him to do. The past decade in thyroid research has been dominated by the radioactive isotopes of iodine and by the chromatogram; and the ever more widespread use of these instruments throughout the world has led to a good deal of repetitive experiment. Now, however, there are indications that the limit of purely isotopic investigations has been reached. No further great discoveries are likely to be made by poring over obscure smudges on the autoradiographs of chromatograms; and most people are realising that valid quantitative deductions cannot be reached by throwing isotopes into physiological pools of unknown dimension. Isotopic activities must be related to chemical data for metabolic processes to be accurately studied. Where a chemical compound exists in two pools, only one of which is accessible to chemical determination, the isotopic technique enables us to transfer information about the pool we can measure chemically to the one which we cannot. For instance, the concentration of iodide in the plasma is too low for direct chemical measurement to be acceptably accurate. If, however, radioactive iodide is administered and allowed to equilibrate, we may assume that the iodide in plasma, urine, and saliva will come to have the same specific activity. Since iodide in urine or saliva can readily be measured chemically we can arrive at a figure for the level of plasma-iodide, in chemical terms. This technique has direct relevance to clinical medicine. If simple goitre in this country is caused by iodine deficiency (or by renal or other losses of iodide) the plasma level of iodide in the goitrous would be expected to be low relative to that in the non-goitrous. If this expectation were confirmed, the case for iodising our salt would be greatly strengthened. On the other hand, the finding of normal iodide levels would point to alternative explanations, such as goitrogens in the diet or inherited partial enzyme defects.

Used in a similar way, the combination of isotopic and chemical techniques enables estimates to be made of the absolute rate of iodide uptake by the thyroid, and of the rate at which organic iodine is leaving the thyroid. A surprising outcome of the application of these

1. *Ann. N.Y. Acad. Sci.* 1960, **86**, 311.
2. *Brit. med. Bull.* 1960, **16**, no. 2.

combined techniques is the claim [3 4] that 30–50% of the stable organic iodine in normal plasma is in the form of mono- and di- iodotyrosines. In the same study (as in countless others) practically no labelled iodotyrosines could be detected in the same chromatograms after administration of ^{131}I. Dr. S. C. WERNER courageously yet temperately put these findings before the goitre conference, and evoked the expected protests from scandalised biochemists. It is indeed hard to contemplate these findings without dismay, since they imply that there exists in the body a vast, inert sea (" pool " would be too puny a word) of iodotyrosines—a concept which is virtually irreconcilable with current views on iodine metabolism. Obviously the chemical methods used in this study will have to be scrutinised with particular care before such a revolutionary claim can be accepted—all the more since the delicate catalytic technique of iodine determination is notoriously susceptible to a wide range of interfering agents. Certainly, however, this claim should be fully and fairly considered.

Another innovation has been the intrusion of immunological techniques into thyroid research. The original observation [5] was a simple one: that the serum of patients with Hashimoto's thyroiditis usually contains antibodies directed against human thyroglobulin; and this evoked the equally simple hypothesis that these antibodies resulted from the escape of colloid into the circulation, and in turn caused the destructive changes within the thyroid. Further work rapidly increased the complexity of the picture. Thyroglobulin itself is now regarded no longer as a single protein but rather as a complex of related substances; nor is it by any means the only thyroid antigen against which antibodies are formed in Hashimoto's disease. The pathological significance of these several antibodies is uncertain: they could equally well be represented as the result or the cause of the thyroid damage. As with isotopes, there seems little doubt that a considerable advance would ensue from linking these immunological studies with chemical determinations. But at the moment none of the thyroid antigens can be described in chemical terms, and indeed the ascertainment of their precise structure is likely to be a formidable task.

The more purely clinical papers at the conference centred for the most part on endemic cretinism and thyroid cancer, with a glance at the intractable problem of exophthalmos. Endemic cretinism was a useful topic, particularly as most members of the two largest delegations—those from Britain and the U.S.A.—had never seen a case. The most striking fact about this bizarre but ill-defined condition is that in many countries it is fast disappearing—in one part of Switzerland no patient with this disorder could be discovered who had been born after 1910. An interesting, but unresolved, problem is the relation of endemic cretinism and deaf-mutism to the analogous genetically determined conditions which have been described here and in the U.S.A. Are the endemic diseases to be regarded as phenocopies of their sporadic analogues, and, if so, at what point in the metabolic chain of events do they link up? It will be a pity if these and similar questions cannot be answered before endemic cretinism disappears: they invite international cooperation in combined expeditions to the remote areas where endemic cretinism still lurks.

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Annotations

NEW PLANS FOR RESEARCH

IN the 47 years since it started as the Medical Research Committee under the National Health Insurance Act, the Medical Research Council has come to occupy one of the key positions in medicine; and the developments foreshadowed in this week's report [1] are of more than usual interest.

Though for preclinical work it has its own National Institute for Medical Research, the M.R.C. possesses no comparable centre for clinical investigation, dividing its clinical units between widely scattered hospitals. It has now come to the conclusion that, though the unit system must remain an essential part of its arrangements, this is, by itself, not flexible and adaptable enough to meet the foreseeable requirements of a changing situation. " In particular the very fact that Council Units are housed in or alongside university or hospital departments has made it increasingly difficult, and indeed impracticable, to consider bringing together several Units in one place for a concerted attack on a major problem, or to develop particular Units to the size that seemed desirable ". Because success often depends on having " a suitable concentration of contiguous disciplines and men in one building ", the Council has decided to set up a clinical research centre of its own. Believing that to build a special hospital for research purposes would be inappropriate in this country, and that a research centre should keep in touch with day-to-day medical practice, it proposes that its new institution should be " incorporated within a general hospital which was providing, and would continue to provide, a full range of services to the community ". The siting, organisation, structure, and staffing of such a centre will present formidable problems, and its realisation will be costly; but the Council feels sure that, besides developing its present means of promoting research, it ought now to create such additional and different facilities.

Whereas in this respect the Council's new policy is centripetal, another of its proposed innovations—the " research group "—is centrifugal. At present the Council supports research either by employing its own staff, who mostly work in M.R.C. research units or at the National Institute for Medical Research, or by giving temporary research grants to investigators at universities and hospitals. For some time, however, it has felt that there is sometimes a case for giving support over a longer period, and it proposes in future to give grants to research groups for work, in a university or other department, which does not need a specially created research unit.

Research in tropical medicine has always been of concern to the Council both as a subject in its own right and as a complement to investigations in temperate

1. Report of the Medical Research Council for the Year 1958–1959. H.M. Stationery Office. 1960. Pp. 330. 1s. 6d.

climates. Of late years new requirements have emerged, partly through changes in the medical needs of people living in the tropics and partly from alterations in the political status of overseas territories. Because of these changes, the whole question of the organisation of research in tropical medicine has had to be reconsidered, and the Council is now to take general responsibility for promoting and coordinating all such research "in so far as this directly or indirectly concerns this country". To this end it will set up, on the analogy of the Clinical Research Board, a Tropical Medicine Research Board. This will take over the work of the existing Colonial Medical Research Committee, including the promotion of visits abroad by experts and by home research-workers who have a problem that could be developed with benefit overseas. The report outlines arrangements intended to produce a career-structure which will command the confidence of medical research-workers. "The opportunities for advancing medical knowledge in the tropics", the Council rightly says, "are vast. This is so not only in relation to those diseases which, although commonplace in this country, occur in different circumstances, or with variations, overseas. In many branches of medical research, the experience and opportunities available in the tropics are such as could not fail to enrich and deepen knowledge, both general and individual".

CONGENITAL MYOPIA

MYOPIA can be divided into three types—simple, progressive or degenerative, and congenital. The first two groups develop during childhood, usually after the age of 4 years (though sometimes degenerative myopia has an earlier onset), whereas the congenital type is present at or soon after birth.

Simple myopia usually varies from 0 to 6 dioptres. It is classified in the biological series of refractive errors and involves no pathological changes.

Degenerative myopia is now thought to be genetically determined. Commonly it progresses to chorioretinal degeneration and sometimes to retinal detachment. In the worst cases blindness ensues in middle age.

Congenital myopia includes several groups of disorders, some non-progressive and others leading to degenerative changes.

Congenital myopia is sometimes accompanied by obvious congenital defects, such as posterior staphyloma, coloboma, albinism, or generalised growth anomalies associated with defects of the pituitary gland or the gonads. In other cases the myopia is found in children who have been prematurely born, as a manifestation of mild retrolental fibroplasia [1–3]; the myopia varies from 2·5 to 20 dioptres and is usually non-progressive during childhood. Cases have also been described in small premature infants where there is no retrolental fibroplasia and no family history of myopia.[1 3 4] Drillien [5] has stressed the high incidence of congenital myopia in infants of very low birth-weight. Of 43 children who had weighed 3 lb. or less at birth, 11 were myopes and most were of poor mental ability.

Often myopia is present in small premature infants in the early weeks after birth, and the vision reverts to normal by 3 to 6 months. Whether congenital myopia is sometimes due to persistence of immaturity of the eye into childhood is unknown. Further work is needed on the nature of the myopia, to determine whether it is due to changes in the cornea, lens, or vitreous, or to an abnormal axial length.

Gardiner and James [6] have lately suggested that maternal disease in pregnancy may be a factor in causing congenital myopia. In a series of 38 cases of myopia of more than 4 dioptres in schoolchildren, they found that 50% of the mothers had had toxæmia, hypertension, or renal disease in the pregnancy ending in the birth of these children, while in a control series of children who had visual defects other than myopia, only 13% of the mothers had had toxæmia or hypertension. There was no association with prematurity in the myopic series, but it is not clear that the myopia was congenital. As Gardiner and James point out, there are indications that fœtal environment is not normal in toxæmia; both blood-flow through the placenta [7] and oxygen saturation in the umbilical vein [8] are reduced. Adequate nutrition in childhood is recognised as a factor in slowing deterioration in progressive myopia; and, conversely, inadequate nutrition in utero might promote congenital myopia. A long-term follow-up of cases of congenital myopia in full-term and premature infants is required before any conclusions can be reached. Cases must be diagnosed in the first 2 years of life, and those with a family history of myopia must be excluded. Such a prospective survey would enable physical and mental defects to be correlated with the clinical history of pregnancy, delivery, and postnatal development.

TIME OF INNOVATION

A BIG factor in the improvement of British hospitals since the war has been the adjuvant action of King Edward's Hospital Fund. Whereas formerly the Fund exerted its influence mainly by distributing money, latterly it has done as much or more by its distribution of ideas. In Mr. A. G. L. Ives, who joined the staff in 1929, it has had as secretary a man who could take fresh views of old situations and could also see what was significant in new ones. To unusual insight he adds the administrator's gift of knowing what should be done next and knowing how to do it; and, though he now has to leave his work prematurely because of the injuries he sustained in the Lewisham railway accident, he must be happy to see so many new branches growing vigorously from the King's Fund stock. The Emergency Bed Service, ably directed by his successor Mr. R. E. Peers, has long been well established. The division of nursing now includes not only the Nursing Recruitment Service but the valuable staff colleges for ward sisters and for matrons. In other departments are the Hospital Catering Advisory Service, the School of Hospital Catering, and the Hospital Personal Aid Service for the Elderly. Perhaps most important of all, there is the Hospital Administrative Staff College, to whose development Sir Wilson Jameson, who has been part-time medical adviser to the Fund, has also given so much thought. In a speech read at the annual meeting on July 13 the Duke of Gloucester spoke truly of Sir Wilson's "invaluable part in helping the Fund in the days of changing circumstances" and expressed "my profound gratefulness to Mr. Ives for all he has done."

Perhaps the highest compliment one can pay to innovations is to suppose that the necessity for them was obvious. Mr. Ives is one of the people who see what will be obvious later, and those who use our hospitals and work in them will long be indebted to him for inconspicuous leadership.

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2. Birge, H. L. *ibid.* 1956, **41**, 292.
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4. McNeil, N. L. *ibid.* 1956, **40**, 24.
5. Drillien, C. M. *Arch. Dis. Childh.* 1958, **33**, 10.
6. Gardiner, P. A., James, G. *Brit. J. Ophthal.* 1960, **44**, 172.
7. Browne, J. C. M., Veall, N. *J. Obstet. Gynæc. Brit. Emp.* 1953, **60**, 141.
8. Walker, J., Turnbull, E. P. N. *Lancet*, 1953, ii, 312.

CARE FOR THE DYING

FOR the Calouste Gulbenkian Foundation Dr. H. L. Glyn Hughes has reported [1] on the care of patients in their last illnesses; and what he says should stimulate interest in this neglected subject. His emphasis on the need for proper facilities for home care is timely, for the impossibility of indefinite expansion of our hospitals is increasingly recognised. Unfortunately home services are far from adequate. The supply of trained workers, including that stalwart support the district nurse, is likely to remain deficient, and so long as we have full employment there will be too few home helps. Dr. Glyn Hughes' proposal that some form of payment should be offered to women for the full-time care of their own kin is sound. Stricter control over nursing-homes for the elderly is also advisable, for some are unsuitable and should be closed. Arrangements for looking after the aged and dying will not, however, be made adequate by any single measure. We must attack the problem on every side: hospital services must be improved and extended, staff in residential homes increased, and voluntary as well as profit-making institutions helped in return for an approved standard of care. As it is, the report is disquieting, and its conclusions and recommendations deserve careful study by doctors and social administrators.

NULLIUS IN VERBA

Ac ne forte roges, quo me duce, quo lare tuter,
Nullius addictus iurare in verba magistri.

(And do not ask, by chance, what leader I follow or what godhead guards me. I am not bound to revere the word of any particular master.)

THE Royal Society's resolute motto, taken from these lines of Horace, catches the spirit of the men who founded the society three hundred years ago—"a society for promoting Physico-Mathematical Experimental Learning", to which Charles II granted a royal charter of incorporation in 1662. The achievements of the society from that day to this have been recalled and revered during this week's tercentenary celebrations.

The Queen, accompanied by the Duke of Edinburgh, went to the Royal Albert Hall on Tuesday to open the celebrations. Her Majesty said she had been much impressed by the foresight which Charles II and his advisers had shown in framing the society's charter, for it had stood almost unchanged. She congratulated the society on its tradition of tireless curiosity, well guarded by succeeding generations; and "as a token of my continuing interest in your work" the Queen presented to the society a silver bell. King Gustav of Sweden was formally admitted to the fellowship and signed the charter book given by Charles II.

In his tercentenary lecture, Sir Cyril Hinshelwood, the president, remarked that some philosophers of history would maintain that the Royal Society had to come into being when it did because the climate and temper of the age demanded it. None the less, all honour to the men who had met the need—Brouncker, Boyle, Moray, Wilkins, and their associates—for if the individual did not in fact determine the event he profoundly influenced the manner of it.

Reflecting on the effects of resistance to new doctrines, the President recalled how the time scales revealed by geology and biology had appalled those who confused the literal truth of Genesis with the basis of religion and morality. And when the theory of evolution completed the outrage of man's expulsion from the centre of the universe by denying his special creation, resistance rose to its height. The opposition subsided, only to be renewed at intervals against new scientific doctrines (as Dr. Alex Comfort put it last week in our columns, twice in a century the human self-estimate was rudely upset by the work of one man—first by Darwin and then by Freud) and these knocks at tradition were bound to generate stern reaction. Yet, Sir Cyril observed, the men of science themselves, as far as could be judged, had numbered about the same proportion of religious believers as the generality of people. Nor had they been conspicuously less well endowed with kindness or morality. Indeed an assurance that ultimate values of goodness and beauty could never be shaken by the pursuit of truth, wherever it might lead, was perhaps the sign of a robuster faith than was shown by recoil from every new and seemingly disturbing fact.

Scientific investigation needed material ways and means, and the further knowledge advanced the more lavish became the scale. The individual in isolation became, except under rare conditions, correspondingly impotent. But the community as a social and political whole could not be expected to possess the detailed understanding to support him. Nor with the tremendous issues at stake today could it remain indifferent. What must be created therefore to mediate between the individual and the major group was a specialised minor community large enough to command prestige and confidence but with membership confined to those who placed the claims of knowledge first.

Specialised organs of the Government were by themselves unsafe, being too exposed to the changing winds of expediency. Universities suffered from the disadvantage that, on the one hand, a given branch of knowledge was divided and scattered among many of them and, on the other, that they had competing preoccupations of importance to them commensurate with that of learning. An academy, therefore, was the natural body to provide for several vital things: non-commercial periodicals for the publication of discoveries; a measure of financial support for ideas still too embryonic to be of immediately obvious practical application; the mutual stimulus of association and discussion; and the immaterial reward of honour for intellectual achievement. Governments could not provide for men of science the intangible yet powerful encouragement which comes from acceptance and election by their peers. The academy, if it maintained high standards of unquestioned impartiality, set the tone throughout the scientific community, and its influence was felt in every quarter. It was no rival to Government organisations or to industry, and should maintain the closest connections with them by electing into its number the leaders from both. Because men of action and men of authority esteemed it an honour to be elected, the academy exerted its influence far beyond the confines of the learned world. The professional men of science heard of the needs of the State and of industry which in their turn were irrigated by the currents of scientific thought. The intercourse on terms of equality between the representatives of these different estates of the nation was like a sensitive nervous mechanism endowing the community which possessed it with capacities and potentialities realisable in no other way. The subtle coordinating action of an academy could no more be replaced by a bureaucratic organisation or a

1. Peace at the Last. 1960. Pp. 63. 5s. (Calouste Gulbenkian Foundation, 3, Prince Albert Road, London, N.W.1.)

system of economic incentives and deterrents than the intricately evolved biological controls of a living organism could be replaced by crudely devised mechanical appliances. And as Nature herself took infinite pains over the perpetuation of the species, making this indeed in most respects her first concern, so the right choice of its members was a matter demanding the most anxious care of the academy, and was perhaps the most important thing it had to do. This was the conception of the Royal Society—that it should mediate between the individual and the community, depending on the loyalty of the one and on the sympathetic understanding of the other.

About 250 official guests are attending this week's proceedings, representing national academies of science, universities, and other organisations in nearly 50 Commonwealth and foreign countries. There are to be ten tercentenary lectures, and the lecturers include Prof. C. D. Darlington (Chromosomes and the Theory of Heredity), Prof. P. B. Medawar (Problems of Transplantation), and Prof. A. L. Hodgkin (Physics and Chemistry of Nervous Conduction). To commemorate the event, the Universities of Oxford, London, and Cambridge are conferring honorary doctorates of science on some official participants in the celebrations. Among those to be honoured are Sir Macfarlane Burnet, the virologist, Sir John Eccles, the physiologist, and Prof. B. A. Houssay, representing the Academy of Sciences of Argentina.

STAPHYLOCOCCAL ENDOCARDITIS

SINCE a report of 9 cases by Fleming and Seal,[1] staphylococcal endocarditis has been recognised as a complication of cardiac surgery—though the disease may arise also in other ways. Lisan et al.[2] have reviewed 38 cases observed at one hospital in Philadelphia between 1949 and 1958 and conclude that its incidence has increased with the general rise in hospital staphylococcal infections. In common with others,[1 3] Lisan et al. found that cardiac surgery was the commonest predisposing cause, and all but 2 of their 38 patients had congenital or rheumatic heart-disease; of these, 21 had undergone cardiac operations, usually for correction of rheumatic valvular deformities. The mortality in the whole series was 37%, which is rather lower than that in most other series [4 5] and similar to that of the commoner *Streptococcus viridans* endocarditis; but during the last five years under review the mortality rose to 70%, presumably owing to infection with resistant organisms.

As in all cases of bacterial endocarditis, early diagnosis and adequate treatment is of the utmost importance. Most reports emphasise the lack of any clear-cut clinical picture. Lisan et al. did not observe splinter hæmorrhages, clubbing, Osler's nodes, or petechiæ in any of their patients, and splenomegaly was unusual; this confirms the earlier findings of Fleming and Seal,[1] and of Denton et al.[3] Shubin et al.[6] found neither clubbing nor splenomegaly among 27 patients, and a murmur was not invariably present in the early stages. Resnekov [7] however, in a series of 10 cases found clubbing in 5, Osler's nodes in 3, and splenomegaly in 2; so it seems that the classical features may sometimes be present. What is important is that their absence in no way denies the diagnosis, which may be hopelessly delayed unless the clinician is on the watch for bacterial endocarditis in patients with unexplained fever, possibly accompanied by congestive failure, particularly in those who have undergone cardiac surgery. Repeated blood-cultures are essential; and the growth of a coagulase-negative staphylococcus should not be lightly ascribed to contamination, since this type of organism has been repeatedly shown to be capable of causing the disease.[1 2 3 7]

No hard-and-fast rules can be laid down regarding treatment, which will ultimately depend on the sensitivity of the causal organism; but Finland [4] has emphasised that two antibiotics should always be used simultaneously to minimise the chances of resistance developing, and penicillin in large doses is probably best used initially in combination with erythromycin or chloramphenicol. Lisan et al. point out that in-vitro sensitivities do not always correlate with the clinical response, and in their experience massive doses of penicillin—up to 50 million units daily—alone or in combination with other antibiotics, produced the greatest number of cures. Difficult cases may require treatment with vancomycin or ristocetin, with which good results have been reported.[8 9] These antibiotics are extremely powerful but unfortunately require intravenous administration and are not without toxic effects. Nevertheless their use is certainly indicated if the infection does not respond to other antibiotics.

ADDISON CENTENARY

LIKE many documents now famous, the monograph *On the Constitutional and Local Effects of Diseases of the Suprarenal Capsules* created little stir when it first appeared. Yet this work, it has been fairly claimed, entitles its author, Thomas Addison, to be known as the founder of modern endocrinology. His right to this title was ably demonstrated by Sir Charles Dodds in the 14th Addison lecture, given at Guy's Hospital on July 13. Sir Geoffrey Marshall took the chair on this occasion, which marked the centenary of Addison's death. Sir Charles depicted the limited potential and resources of medical inquiry in 1860 (the ophthalmoscope did not come into general use until twenty years after Addison died); and he went on to trace the remarkable developments that sprang with increasing momentum from Addison's clinical observations and the complementary physiological researches of Claude Bernard. One of the latest items in this story was enacted in Sir Charles' own department—the identification of aldosterone by Simpson and Tait.

THE WELLCOME TRUST

SINCE the death of Sir Henry Wellcome in 1936 the trustees of his Will have been operating as The Wellcome Trust. Sir Henry Dale, O.M., the senior trustee, has been chairman for twenty-two years. Having now reached the age of 85 he has retired from the trusteeship, though he will retain his connection with the Trust's activities in an advisory capacity. Lord Piercy has succeeded him as chairman.

Sir ARTHUR PORRITT has been elected president of the Royal College of Surgeons of England in succession to Sir James Paterson Ross.

1. Fleming, H. A., Seal, R. M. E. *Thorax*, 1955, **10**, 327.
2. Lisan, P., Uricchio, J. F., Marino, D. J., Deshmukh, M., Likoff, W. *Amer. Heart J.* 1960, **59**, 184.
3. Denton, C., Pappas, E. G., Uricchio, J. F., Goldberg, H., Likoff, W. *Circulation*, 1957, **15**, 525.
4. Finland, M. *ibid.* p. 641.
5. Wilson, R., Hamburger, M. *Amer. J. Med.* 1957, **22**, 437.
6. Shubin, H., Levinson, D. C., Griffith, G. C. *J. Amer. med. Ass.* 1958, **167**, 1218.
7. Resnekov, L. *Lancet*, 1959, ii, 597.
8. Geraci, J. E., Heilman, F. R., Nichols, D. R., Wellman, W. E. *Proc. Mayo Clin.* 1958, **33**, 172.
9. Romansky, M. J., Holmes, J. R. *in* Antibiotics Annual, 1957–58; p. 187. New York.

Points of View

NOT YET . . . ?

THE recent House of Commons debate [1] on the Wolfenden report cannot have encouraged those who favour reform of the law concerning homosexuality. In spite of a three-year campaign conducted by the Homosexual Law Reform Society and in spite of the twelve out of the thirteen members of the Wolfenden Committee who recommended changes in the law, the motion calling on the Government to take early action to carry out the committee's recommendations was supported by less than a sixth of the membership of the House, having been defeated by a two-to-one majority in a half-empty House.

The debate was unconstructive, though on this occasion the prospects of the reformers had looked good in advance. There was a widespread impression that more serious public opinion had taken a decided turn in favour of reform, especially in religious circles. The Archbishops of Canterbury and York, the Church Assembly, the Methodist Conference, and the committee set up by the Roman Catholic Church all supported the Wolfenden recommendation; and editorial opinion had been heavily in favour, too, in that section of the Press read by the more responsible sections of the population. The *Observer* remarked that " the house remains to a great extent ignorant of the social realities of homosexuality ", and the opponents of the motion appeared to have no difficulty in disregarding completely both the considered opinion of years of study in the Wolfenden report and responsible religious opinion too.

* * *

The publication of Mr. Gordon Westwood's report [2] on the life of the male homosexual in Great Britain was timely, but it failed to influence the debate. Mr. Westwood's study, planned by the research committee of the British Social Biology Council, was an inquiry into a sample of 127 homosexual men. It was a courageous piece of work, undertaken in the face of great difficulty, and it deserves very careful attention.

Any inquiry of this kind is bound to have serious shortcomings, which Mr. Westwood both recognises and points out. Any inquiry which depends on a sample of men revealing their own criminal activities can never give a completely accurate picture. It is bound to be weighted on the side of the socially responsible and of those who retain some trust in their fellow men. Obviously the more psychopathic and disturbed members of the homosexual population will be very shy of coming forward, even if they can be contacted at all. Despite these difficulties, the sampling, in respect of spread of age, occupation, social class, and the other usual sampling criteria, easily stands comparison with other social inquiries, which is also true of the statistical handling of the findings and of the cautiousness of the interpretations. Whatever its shortcomings, this report is the most impressive study of the subject that has yet appeared.

No surprising new facts emerged, but there is confirmation of many views previously based on clinical and practical impression. Among the more important findings it was concluded that homosexuality is to be found in all walks of life, and no significant clusters appeared other than the well-known drift to big centres of population and, allegedly, to certain districts in big towns. About half of the sample remained well integrated in social life, living lives that were normal in respects other than sex life, useful citizens contributing to society. The other half showed various degrees of social disability; but four-fifths had never come into contact with the law for any reason. There is no evidence that homosexuality is associated with the committing of other offences, but, as is well recognised, it attracts blackmail, which is a potent source of suffering to homosexuals. The making of contacts in public is only a small part of homosexual behaviour, mainly restricted to the inexperienced who have yet to form regular habits of association, together with the rogues and blackmailers who prey upon them. As the law operates at present it is predominantly the inexperienced that get caught by the setting of traps in public lavatories, and the like. This is serious because conviction for homosexual offences tends to drive homosexuals into homosexual coteries and thus to widen the gap between them and normal society. In about 90% of police charges, a confession is obtained—which is remarkable for offences committed in private, when no direct evidence is obtainable. Methods used by the police include the building of intricate chains of circumstantial evidence based on questioning, offers of assistance if an admission is made, and extensive if intermittent use of plain-clothes methods of detection, not excluding the use of *agents provocateurs*. This is perhaps the least reliable part of the report, but few observers doubt that the operation of the law in this respect is capricious, to say the least, which is a serious state of affairs, if true, when it applies to at least 4% of the population—say, 750,000 men.

The report throws little light on causation, but it is noted that a significant proportion had inadequate homes as children and many suffered separation from their fathers for long periods. Perhaps later researches will focus on the quality of relationships that homosexuals had with their mothers during childhood, though this will be a hard task to undertake retrospectively. The first homosexual experiences were not found to have a significant connection with the later development, and the report concludes that effects of seduction and early experiences with adults seem to be exaggerated. On the other hand, the social relationship between an adult homosexual and a boy may be important. A third of the sample were living in long-term regular associations with other individuals, a third had had long-term associations in the past; and a third had never had an emotional alliance lasting more than a year. Promiscuity was found to some extent in two-thirds of the sample, but the report notes that fear of the law caused many homosexuals to restrict their sexual activities to anonymous single contacts.

About a fifth of the sample had had some heterosexual experience, but usually slight or intermittent. About two-thirds, however, had had a regular girl-friend whom they had met fairly often for a year or more; but half of these claimed that they had not experienced sexual attraction. Most of the sample seemed to have come slowly, often reluctantly, to the conclusion that they were homosexual during the late teens and early twenties. Those who succeeded in coming to terms with their deviation were not longer interested in obtaining advice or treatment. There was almost unanimous condemnation, among the group, of male prostitution; and the great

1. See *Lancet*, July 9, 1960, p. 92.
2. A Minority. By GORDON WESTWOOD. London: Longmans, Green. 1960. Pp. 208. 30*s*.

majority appeared to dislike the feminine characteristics of some of their number. Strong preferences were expressed for those who have a manly appearance and masculine interests and there was much criticism of the flaunting of clothes and attitudes. As far as this group is concerned, the " pansy " is regarded as an outsider. Very few adult-seeking homosexuals are sexually interested in pre-pubertal boys, and pædophilia seems to be a separate phenomenon.

The behaviour of this sample conflicts with the enormous distinction made, both by the law and by the uninformed " normal " public, between gross indecency and buggery, respectively. Many contacts were prepared to try most of the techniques, but less than a third regularly participated in anal intercourse. Nor was it possible to make a clear distinction between active and passive homosexuals.

Mr. Westwood throws particular light on some of the social phenomena of this group. For instance, it is noted that homosexual groups show many of the characteristics of minority groups, especially perhaps of persecuted minorities. The social pressures act as a progression from early feelings of social isolation to complete absorption in the homosexual way of life. Much undesirable public behaviour seems to stem from the fact that homosexuals find it socially impossible to establish a stable form of private home life. On the other hand, many show aspects of minority behaviour such as filling houses from among their own number, protecting each other's employment interests, and developing strong intra-group loyalty that leads also to the provocative display of group idiosyncrasies in many cases and, to some extent, to revengeful and other antisocial attitudes and acts. This is common ground with other minorities and as always it tends to call down majority group retribution. So-called proselytism is a case in point. It is reported that almost 19% of the sample try to obtain partners who are not homosexual, but the reader may infer that these partners will be bi-sexual rather than truly " normal ". The report is inconsistent on this important issue: in one place it is stated that assertions that homosexuality is a proselytising religion do not rest on scientific evidence. All that can be said, strictly, is that some men with only slight overt homosexual tendencies are persuaded to engage in homosexual activities. Elsewhere, in the summary, the report states that there is some foundation for the contention that homosexuals attempt to proselytise—a statement selected by an opponent of law reform for damaging use in the Commons debate.

The fact is that nothing is known of the effects of such persuasion. Do these bi-sexual partners go over to homosexuality? Do they significantly increase their homosexuality at the expense of their heterosexuality? Nobody knows. On the other hand, it is known that two-thirds of the sample had in the past been subjected to a potentially proselytising influence in the other direction, that of their regular girl friends; and 18% had taken part in heterosexual intercourse to a significant extent, but without a major change in their sexual polarity. It is not justifiable to assume without evidence that seduction in one direction is more permanent in its effects than in the other. In other words, there is no scientific evidence that proselytism is an important consideration.

* * *

The medical reader may well feel concern at the apparently poor showing of the medical profession in the eyes of the homosexual. In the case of general practice this may not cause surprise because no part of medical training is specifically designed to help the doctor with the understanding, let alone the treatment, of this condition. 12% of Westwood's sample had had treatment from a psychiatrist; half gave up in less than three months but the remainder were reasonably satisfied with the outcome. Clearly much remains to be done before medicine can claim to be making an effective contribution to the solution of the problem.

Lack of medical confidence was reflected in the memorandum submitted by the British Medical Association to the Wolfenden Committee, in which, according to Mr. Westwood, the moral emphasis was at least as great as the medical. The doctors tended to advocate religious conversion rather than medical treatment as a cure for homosexuality; whereas in the corresponding report of the Church of England Moral Welfare Council a serious warning was given about the clinical difficulties in the way of effecting cure by religious means.

In view of medical uncertainty, it is unfortunate that many doctors and perhaps the overwhelming majority of the less sophisticated public think of homosexuality as a disease, albeit a moral disease. This is analogical thinking, because there is no agreement on the nature of the pathology. As often happens, the fears and fantasies aroused by the analogy have tended to run away with objectivity.

Possibly the majority of the public are trapped by the analogy and feel, rather than think, that homosexuality is highly contagious, extremely destructive, and, in the 18th-century sense, mortifying. In such a way, medieval people regarded leprosy; and seventeenth-century people, the plague. Others, with a more collective turn of thought, regard homosexuality as a kind of cancer, remorselessly infiltrating and destroying the body of society. In both instances the tendency is to react with horror, disgust, and fear to the evidence of the ravages of the " disease ". Therefore, it is not surprising that there is an insistent clamour from numerically large sections of the public that the " disease " be treated by the crude public-health techniques of isolation, control of contacts, disinfestation, disinfection, and, above all, destruction of the noxious agency. Inasmuch as the agency is confusedly thought to be morally responsible for its own toxicity and malignancy, there is an insistent demand for retribution and punishment.

There are some who react less emotionally to homosexuality and who often consider that homosexuality is a developmental deviation. Since the means of recognising the deviation before adult life are inadequate, it may be concluded that the process is irreversible, that the most that can be attempted is to restrict the harm that may ensue, by whatever institutional means are available. There is only a short distance between this attitude and therapeutic nihilism.

A third type of analogy that is sometimes used, and which offers a prospect of clearer thinking, if not more hope, is that of the deficiency disorder. It can be argued that homosexuals show in common a deficiency in capacity to form interpersonal relationships of the kind that can sustain a durable love relationship with a member of the opposite sex. In rickets a deficiency exists that impairs bone formation, and this, one might claim, is the limit of the disease process; but a disturbed pattern of

growth and physical (mainly mechanical) pressures cause gross deformity. Thus the bony structure becomes misshapen and all the attendant disabilities follow.

It does not force the analogy to suggest that in the case of the homosexual, too, it is the disturbed pattern of emotional growth due to deficiencies in relationship formation, combined with severe social pressure, that do the actual damage. Just as it is impossible to straighten rachitic curvatures by mechanical means alone, so a direct attack on behaviour can scarcely succeed in homosexuality. Much can be done, however, to help the cripple to learn to live with his deformity, and, provided expectations are not unrealistic, the homosexual can be helped too; but hardly through increasing the social penalties and pressures under which he lives, by branding his deformity as a criminal offence. And, lastly, while no doctor would attempt to cure rickets by giving vitamins and withholding calcium, it was suggested in Parliament that attempts should be made to deal with the relationship deficiency by psychotherapy in prison, while withholding any opportunity for relationship formation, with either sex.

Clearer recognition both by doctors and by the public that this complicated problem of homosexuality has dual aspects of relationship deficiency and subsequent character distortion would enable more appropriate and more adequate diagnostic and therapeutic efforts to be attempted. It would also help all parties to avoid the pitfalls, on the one hand, of entertaining unrealistic expectations of cure of the deformity while the underlying deficiency remains unrecognised and therefore unpreventable; and, on the other, of cynical nihilistic attitudes because the fully formed deformity proves stubbornly resistant to direct measures.

* * *

The path to law reform by Parliamentary debate now seems to be blocked, for some years at least. The recent debate in the House of Commons, as reported in *Hansard*, is a powerful corrective of easy optimism over what can be done in the immediate future to straighten out this tangled situation. Perhaps the supporters of the motion made a miscalculation in hoping that the lesson of the important evidence presented to the Wolfenden Committee had been generally assimilated.

It is discouraging to read the by now almost traditional but still unfounded assertions made during the debate: for example, that homosexuality is on the increase; that it is actively proselytising; that homosexual seduction is a severe danger to the young; that ceasing to punish homosexual acts between consenting adults in private would result in an enormous increase of homosexuality; that repeal of this enactment would set society's seal of approval on " vice " and open the flood-gates to licentiousness.

On the other hand, no serious attempt was made to justify the present law. Most of the speakers acknowledged that, sooner or later, a change must come, but in their opinion the time was not yet. The usual fears were expressed about what might happen if the Labouchere amendment (a clause introduced in the report stage of the Criminal Justice (Amendment) Act of 1885, making gross indecency between consenting adult males in private a criminal offence) were repealed. No account was taken of the experience of other countries in this regard. Western Germany is the only other European country which still retains this offence, and no country has reported any social problem arising from its abolition. In the debate a deeper, if more primitive level of anxiety about sexual behaviour was pithily expressed by one member whose only contribution to the debate was to ask: " If we are to allow this sort of thing to occur, would my honourable Friend be happy to go into a public house and find a couple of hairy old males sitting on each other's knees and liking it ? Is that what we are going to allow ?"

In fact all fears raised in the Commons had been taken into consideration by the Wolfenden Committee during the framing of the report.

The Home Secretary wished to make three preliminary conditions before promising action: first, research; second, education of public opinion; and third, acknowledgment by those who speak of these matters that there is a difference between sin and crime, and by those who attempt to reform the law that homosexuality is, in general, an undesirable practice.

The Government's plans for research consist of a project under the auspices of Birkbeck College to compare the psychological and other characteristics of homosexuals with those of non-homosexuals, using a sample of homosexuals who have been convicted of homosexual offences or have been treated in clinics because of such tendencies. A second line of study, not specified, is to investigate the nature of homosexual groups, taking particular note of the means by which and the extent to which homosexual conduct spreads in society. A third plan is to study the possibility of influencing homosexual behaviour by psychotherapy or medical means(sic), such as the use of œstrogens. Mr. Butler implied, though he did not actually state, that this last project was being carried out on a prison population, and he mentioned the new psychiatric hospital at Grendon Underwood.

It is hard to see what can be hoped for from a programme of research of such modest dimensions directed at such a small and arbitrarily selected sample of the 750,000 or so adult homosexuals in this country who at present stand in the shadow of the criminal law—to say nothing of the corresponding number of boys under the age of 15 who, presumably, will be the homosexuals of the next generation. Not only is the programme itself totally inadequate in size; but it is apparently put forward in the supposition that it is possible to carry out a reliable investigation, under Home Office auspices, into criminal behaviour. There is a vicious circle here of the most stubborn kind. On the one hand it is stated that the law cannot be changed until more research is done and more scientific knowledge gained; on the other hand, scientific research cannot be underaken properly until the law is changed and until the subjects of the research project are relieved of the consequence of becoming self-revealed criminals. Until the law is changed, the research population will consist of two groups only: those whose social integration is sufficient for them to trust the sponsors of the research; and a captive population made available by the working of a law that was described in Parliament as " capricious ". In neither case can the true significance of the sample be known, nor the validity of applying findings to the community as a whole. Mr. Westwood has effectively shown both the possibilities and limitations of work with the first group, and it is not adequate merely to plan repetitions of studies of an undefinable sample of the whole. The urgency of the human problem demands a courageous approach and clear-thinking leadership.

KENNETH SODDY
M.D., D.P.M.

Occasional Survey

VIRUS TUMOURS OF MICE

AFTER Bittner's discovery of a mammary tumour agent in mice in 1936 [1] no sustained claim to have detected causative filterable agents in mammalian tumours was made until 1951 when Gross [2] reported that he had induced leukæmia by injecting filtered extracts of leukæmic tissue into mice within 16 hours of birth. This report and subsequent publications [3] stimulated a large amount of experimental work which has led to the identification of Friend's leukæmia virus [4 5] and of the P or polyoma virus.

There was much confusion between these three conditions.[6] The first to be recognised as a separate entity was Friend's leukæmia,[4 5] found in Swiss mice during serial propagation of the Ehrlich ascites form of adenocarcinoma. In young Swiss mice inoculation, first, of cell-free ascitic fluid and later of filtrates made from leukæmic spleens raised the white-blood-cell count from 50,000 to 300,000 per c.mm. in five to seven weeks. Usually 85% or more of inoculated mice died in thirty to a hundred days. Filtrates were stable for long periods at −70°C or when freeze-dried. They were inactivated at 56°C for thirty minutes. Specific neutralising antisera which prevented infection were made in rabbits and mice. Normal sera from other sources or from patients with leukæmia did not neutralise the agent; but formolised vaccine made from filtrates gave significant protection. On morphological grounds Andervout et al.[7] considered that the condition would make a laboratory prototype for human infectious mononucleosis—a contention disputed by Gross.[8] Infective mononucleosis is a self-limiting condition: when inoculated, Friend's leukæmia is usually lethal.

In an early publication Gross [9] reported that, instead of the expected leukæmia, some young inoculated mice developed bilateral parotid tumours and subcutaneous sarcoma in response to leukæmic filtrates; and Stewart [10] had a similar experience.

The leukæmia produced with filtrates by Gross, unlike Friend's leukæmia, is seldom a blood-cell disease of the circulation. It consists in enlargement or lymphosarcoma of the thymus with an enlarged white mesenteric lymph-node, and enlarged spleen, liver, and regional nodes. The parotid tumour is a myoepithelioma of the mouse salivary gland similar to foci sometimes seen in the human disease but unlike most examples.[11]

Hitherto, spontaneous parotid tumours provide the only known morphological evidence of naturally occurring infections of mice associated with a filterable agent found by Stewart and her colleagues.[10 12] The agent, which is present naturally in many mouse colonies, is known as the parotid, P, or polyoma virus (the last on account of its pluripotent tumour-inducing capacity under experimental conditions). For a time it was confused with the leukæmia agent of Gross. After multiplication in cell-culture of the agent which causes these tumours,[12] newly born hamsters [13] and rats can be infected, with production of kidney sarcomas—thus transcending the barrier of species specificity. The distinction, long suspected, between polyoma and leukæmia was made in the course of an epidemiological study of various mouse colonies at the National Cancer Institute, Bethesda, by Rowe et al.[14] Prevalence of infection was traced by means of hæmagglutination inhibition in mouse sera. A high-leukæmic colony bred for production, housed outside the laboratory and commonly used as a source of leukæmia, was free of hæmagglutination-inhibiting antibody, whereas high titres were found in varying degree among stocks in individual laboratories; the incidence of antibody was highest where there was artificial contamination of the environment with virus, as by experimental procedures. Filterability of the agent of polyoma, its high degree of infectivity, especially after cultivation in vitro in cells, prevalence in mouse stocks, survival after heating even to 70°C, and rapid tumour-inducing capacity in newly born mice and hamsters have been confirmed many times over. The first report of polyoma as a natural infection in this country appears to be that of Salaman,[15] who obtained a great mixture of tumours when C_3H mice newly born were injected with filtrates of leukæmic material from the Manchester AK mouse strain. In a B.B.C. programme on Dec. 1, 1959,[16] television viewers were shown an enlarged electron microscope picture of this virus which relatively few laboratory workers have seen. It is an astonishingly complex geometrical structure consisting of exactly shaped and arranged subunits. Advances in technique which have revealed so much differentiation in this and some non-neoplastic viruses encourage hope that others may one day be identifiable by structure. At present they look much alike though their infective and pathogenic properties may be very different.

The identification of polyoma virus and its tumours, together with realisation that to obtain Gross' leukæmia with certainty his procedures must be precisely followed,[17] has cleared the way for what may be even more arduous tasks—deciding whether or not his leukæmia is viral in origin and whether it is unique among leukæmias. Only in $C_3H/_{Bl}$ mice derived from Bittner's subline do young mice respond regularly by developing early leukæmia. In other strains, even other C_3H sublines, results are erratic or completely negative. Doubts concerning a viral cause of this leukæmia were expressed by Andervout et al.[7] and were answered by Gross.[8] The point at issue was the vertical transmission of the disease—that is, the passage from parents infected with test filtrate to their own uninoculated offspring and to their subsequent progeny. Gross admitted that this rarely happened but had been achieved once for one generation and once for five generations, after which spontaneous transmission ceased. Spontaneous loss of an agent, judged by no development of mammary tumours, is known especially in the RIII strain. There is, however, another objection to a virus cause, based on differences of opinion on the natural incidence of leukæmia in the test strain. Whether an incidence of 1·5% as Gross maintains, or 10–15% is

1. Bittner, J. J. *Science*, 1936, **84**, 162.
2. Gross, L. *Proc. Soc. exp. Biol., N.Y.* 1951, **76**, 27.
3. Gross, L. *Cancer Res.* 1958, **18**, 371.
4. Friend, C. *J. exp. Med.* 1957, **105**, 307.
5. Friend, C. *ibid.* 1959, **109**, 227.
6. See *Lancet*, 1958, ii, 30.
7. Andervout, H. B., Dawe, C., Dunn, T. B., Law, L. B., Potter, M., Stanton, M. F. *ibid.* 1959, i, 154.
8. Gross, L. *ibid.* p. 891.
9. Gross, L. *Proc. Soc. exp. Biol., N.Y.* 1953, **83**, 414.
10. Stewart, S. E. *J. nat. Cancer Inst.* 1955, **15**, 1391
11. Law, L. W., Dunn, T. B., Boyle, P. J. *ibid.* 1956, **16**, 495.
12. Stewart, S. E., Eddy, B. E., Borgese, N. *ibid.* 1958, **20**, 1223.
13. Eddy, B. E., Stewart, S. E., Young, R., Mider, G. B. *ibid.* p. 747.
14. Rowe, W. P., Hartley, J., Estes, J. D., Hubner, R. J. *J. exp. Med.* 1959, **109**, 449.
15. Salaman, M. H. British Empire Cancer Campaign; thirty-sixth annual report, 1958; p. 158.
16. Brenner, S., Horne, R. W. B.B.C. Television. Dec. 1, 1959: Science International.
17. Kassel, R., Rottino, A. *Cancer Res.* 1959, **19**, 155.

the true one may depend on the diagnostic criteria observed and on the survival age when incidence is judged. These details are seldom published. Renewed doubts of the viral origin of Gross' leukæmia have been expressed by Miller,[18 19] who argues that raising incidence and reducing the time of appearance of a tumour by means of filtered cell-free extracts is insufficient evidence that the filtrate contains a causative virus. Also in need of explanation is the fact that leukæmia in mice, whether arising spontaneously or induced by X-irradiation or chemical carcinogens or with Gross' filtrate, is preventable by previous thymectomy. Miller [19] has now found that if, from one day to six months after thymectomy, the unresponsive inoculated mice were grafted with thymus from normal untreated mice, 50–100% of these grafted mice later developed lymphoid tumours. Miller concludes that the potentiality for leukæmia development is still present in inoculated mice for many months after thymectomy. Grafting of normal thymus reveals this potentiality, and the thymus may be the source of a humoral influence. Evidence of a humoral lymphocyte-stimulating factor (L.S.F.) is being gradually built up and has been solidly supported by Metcalf.[20 21] The lymphocyte count in normal mice was increased by the injection of supernatant fluid from normal centrifuged emulsions of human or mouse thymus and to a greater degree when the emulsions were derived from mouse or human lymphatic leukæmia (but not the myelogenous form) or from lymphosarcoma. A rise in L.S.F. in serum precedes the onset of leukæmia, induced experimentally by irradiation or by filtrates. It appears that the situation may be analogous with spontaneous mouse mammary carcinoma in which heritable susceptibility and hormonal factors are required and incidence is increased when mammary tumour agent is present.

The discovery of the polyoma agent with its capacity to induce tumours in a variety of young animals and cells within days or weeks provides a most valuable tool for investigating the change from normal to neoplastic cells. It would clearly be of value to have confirmation of a humoral lymphocyte-stimulating factor and to learn more about its chemical and physical nature.

18. Miller, J. F. A. P. British Empire Cancer Campaign: thirty-seventh annual report, 1959; p. 97.
19. Miller, J. F. A. P. *Brit. J. Cancer*, 1960, **14**, 83, 93.
20. Metcalf, D. *ibid.* 1956, **10**, 169, 431, 442.
21. Metcalf, D. British Empire Cancer Campaign: thirty-seventh annual report, 1959; p. 496.

Special Articles

POISONING BY ORGANOPHOSPHORUS COMPOUNDS USED IN AGRICULTURE AND HORTICULTURE

We have been asked by the Ministry of Health to publish the following note which has been prepared by a medical panel of the Scientific Subcommittee of the Interdepartmental Advisory Committee on Poisonous Substances used in Agriculture and Food Storage.

IN current commercial practice a large number of organophosphorus preparations are widely used both in agriculture and horticulture (including glasshouse crops). In the open, most spraying is carried out between May and September, whereas under glass it may be done at any time of the year.

Those organophosphorus compounds most likely to cause trouble are scheduled in the Agriculture (Poisonous Substances) Regulations. (These include: amiton; demeton; demeton-methyl; dimefox; 'Gusathion'; mazidox; mipafox; parathion; 'Phosdrin'; phosphamidon; schradan; sulfotepp; T.E.P.P.) Nevertheless, the less toxic unscheduled materials could themselves cause poisoning if misused after a more toxic organophosphorus compound had led to symptomless over-exposure—e.g., cholinesterase depression.

Pharmacology

Their fundamental action in man is to depress cholinesterase enzyme activity. Acetylcholine accumulates at the autonomic synapses and at the endings of the post-ganglionic parasympathetic and the skeletal efferent nerves. The toxic effects resemble those of physostigmine (eserine) and neostigmine ('Prostigmin'), but with some compounds may be much more persistent, lasting for a day or two rather than hours. Successive hours or days of unsafe use may cause progressive lowering of the cholinesterase enzyme level.

Toxic Effects

The first symptoms of intoxication are usually anorexia and nausea, often with mental confusion and a sense of unreality. They may be experienced during exposure, or up to eight hours later. Vomiting, cramp-like abdominal pain, excessive cold sweating, and salivation soon follow. Giddiness, apprehension, and restlessness may also be noticeable. (Constriction of the pupil may be seen, but this is not a constant sign of poisoning, nor is it an indication of its severity. It may be caused by the local effect of spray mist in the eye.)

As poisoning progresses, muscular twitchings begin in the eyelids and tongue, then other muscles of the face and the neck become involved. Generalised twitching with profound muscle weakness occurs in severely affected persons, as do convulsions. Later manifestations include diarrhœa, tenesmus, involuntary defæcation, and pulmonary œdema with broncho-constriction. Ataxia, tremor, convulsions, drowsiness, respiratory depression, and mental confusion follow, gradually advancing to coma.

Management and Treatment

Whenever possible, a blood-sample should be obtained (see below) before starting treatment. The skin is, usually, the most important route of absorption. All clothing that might be contaminated should be removed at once and exposed areas of skin (hands, arms, face, and neck) thoroughly washed with soap and water.

At the same time, an injection should be made of atropine sulphate, in the high dose of 2 mg. (gr. $^1/_{30}$), by the intramuscular or subcutaneous route. In mild cases this may be enough in itself. If the symptoms are not promptly relieved or if the condition of the patient deteriorates—e.g., with the development of incipient convulsions or respiratory depression, further atropine is required at frequent intervals (10–30 min.) and a specific cholinesterase reactivator should be given. The use of such an agent becomes a matter of urgency if the patient has failed to respond even after 10 mg. of atropine, as the probability is that, if a specific reactivator is given more than twelve hours after the onset of symptoms, it will not be so effective.

Under no circumstances should atropine injections be delayed until cholinesterase reactivators are available, but should be continued until signs of atropinisation occur—i.e., dilated pupils, dry mouth, and rapid pulse. The patient should be kept fully atropinised and under observation for at least twenty-four hours, preferably in a hospital, and if symptoms return after the cessation of atropine treatment further atropine should be given. Persons suffering from organophosphorus poisoning tolerate more atropine than do normal persons. In severe cases, very large amounts, 100 mg. or more, of atropine may be required over the full period.

It is essential that the cholinesterase reactivator should be given intramuscularly or intravenously as early as possible and preferably at the same time as the atropine. Two such agents are available, namely P2S and P2AM (or PAM). The recommended initial dose of P2S is 1 g. dissolved in 5 ml. of Water for Injection (*B.P.*) which can be used intramuscularly and intra-

venously. Further 1 g. doses of P2S or P2AM (PAM) may be necessary at intervals of three to four hours.

In cases of this emergency, supplies of P2S may be obtained from any of the centres which have been established throughout the country. These are listed below.

Careful watch must be kept on the respiration. With these treatments there should be no respiratory depression. If it does occur, pulmonary ventilation must be maintained by any of the recognised artificial means. Some simple mechanical device—e.g., a positive-pressure bellows resuscitator—will give better results than ordinary manual methods. In severe cases, and especially if treatment has been delayed, there may be excessive mucous secretion, combined with bronchoconstriction, which will tend to block the airway. Care must be taken therefore to keep the airway clear and it may be necessary to pass an endotracheal tube or perform tracheotomy. *This is most important.* The passage of an endotracheal tube and bronchial aspiration should not be delayed if there is any evidence of interference with the airway.

Laboratory Diagnosis

Diagnosis of poisoning by organophosphorus compounds can be confirmed by demonstrating a much-reduced cholinesterase activity in the whole blood, red blood-cells, or in the serum. *A blood test should be made in every suspected case.* For this purpose 5 ml. of venous blood should be taken into a dry syringe, free from spirit, and expelled gently (to avoid hæmolysis) into a tube containing an anticoagulant (e.g., a mixture of potassium and ammonium oxalates or heparin), and shaken gently. It should be sent to one of the laboratories listed below.

A reduced level of cholinesterase activity in the blood indicates that an anticholinesterase chemical has been absorbed. If the depression is marked, the patient will be more susceptible to the effects of further exposure to an organophosphorus compound. Any person who has been detectably affected should not, therefore, be allowed to return to work or to come into contact with any organophosphorus compounds until his whole blood cholinesterase activity has returned to at least 70% normal. The rate of recovery of cholinesterase activity in the blood varies according to the chemical responsible. Complete recovery under certain circumstances may take two or three months. It is therefore advisable for an affected person to have further blood examinations made every seven to fourteen days until recovery has been established.

Supplies of P2S

P2S can be obtained from the following centres:

Region 1. Newcastle
The Pathological Laboratory, Cumberland Infirmary, Carlisle. Carlisle 22332.
The Dispensary, Newcastle General Hospital. Newcastle 35211.
Region 2. Leeds
Castle Hill Hospital, Cottingham, Hull. Cottingham 47372.
Seacroft Hospital, York Road, Leeds. Leeds 648164.
Region 3. Sheffield
Nottingham City Hospital, Hucknall Road, Nottingham. Nottingham 63361.
Region 4. East Anglia
Regional Transfusion Centre, Government Buildings, Brooklands Avenue, Cambridge. Cambridge 56912 (8.30 A.M. to 5.30 P.M. Mondays to Fridays and 8.30 A.M. to 12.30 P.M. Saturdays. Cambridge 56913 at times other than those stated above.
Norfolk and Norwich Hospital, St. Stephen's Road, Norwich, Norfolk, NOR 53A.
Region 5. North West Metropolitan
Edgware General Hospital. Edgware 2381.
Region 6. North East Metropolitan
North Middlesex Hospital, N.18 (Day: Chief Pathologist; night: Resident Pathologist). Edmonton 3071.
Chelmsford and Essex Hospital, London Road, Chelmsford (Dr. J. W. Lacey, Group Pathologist). Chelmsford 3481.
Region 7. South East Metropolitan
South London Transfusion Centre, South East Sub-Depot, David Salomon House, Southborough, near Tonbridge. Day service: Southborough 1480; night service: Maidstone 4463; Maidstone 4660.
Kent and Canterbury Hospital, Ethelbert Road, Canterbury. Canterbury 2291.
Region 8. South West Metropolitan
South London Transfusion Centre, Stanley Road, Sutton, Surrey. Vigilant 8221.
Region 9. Oxford
Northampton General Hospital. Northampton 4680.
Royal Berkshire Hospital, Reading. Reading 81721.
Region 10. South Western
Ham Green Hospital, Bristol. Pill 31165.
Pathological Department, Royal Devon and Exeter Hospital, Exeter. Exeter 73519 (Exeter 72261 when laboratory closed).
Scott Isolation Hospital, Plymouth. Plymouth 64311.
Pathological Department, Royal Cornwall Infirmary, Truro. Truro 3081.
Region 11. Wales
Cardiff Isolation Hospital, Cardiff. Cardiff 21466.
West Wales General Hospital, Clangwili, Carmarthen. Carmarthen 6733.
Aberystwyth General Hospital. Aberystwyth 374.
Caernarvon and Anglesey General Hospital, Bangor. Bangor 1181.
Maelor General Hospital, Wrexham. Wrexham 3512.
Region 12. Birmingham
The Dispensary, Worcester Royal Infirmary, Worcester. Worcester 27122. After 8 P.M.: night superintendent; all other times, matron.
The Dispensary, Royal Salop Infirmary, Shrewsbury. Shrewsbury 2056. Pharmacist on call at the hospital.
The Dispensary, County Hospital, Hereford. Hereford 4201. Medical officer on duty.
The Dispensary, Staffordshire General Infirmary, Stafford. Stafford 753. Medical registrar.
The Dispensary, Selly Oak Hospital, Birmingham. Selly Oak 1361. After 8 P.M.: night superintendent; all other times, matron.
Region 13. Manchester
The Dispensary, Manchester Royal Infirmary. Ardwick 3300.
Region 14. Liverpool
Fazakerley Hospital, Longmoor Lane, Liverpool, 9. Aintree 2342.
Region 15. Wessex
Royal Portsmouth Hospital, Commercial Road, Portsmouth. Portsmouth 2103.
The Dispensary, Royal South Hants and Southampton Hospital. Southampton 26211.
Royal Victoria Hospital, Shelley Road, Bournemouth. Boscombe 35201.

Blood-cholinesterase Estimations

These laboratories can carry out estimations of the *cholinesterase activity* of blood-samples:

Department of Pathology, Memorial Hospital, Peterborough.
Group Laboratory, Lewisham Hospital, Lewisham, London, S.E.13.
Central Laboratory, Milton Road, Portsmouth.
Department of Pathology, Selly Oak Hospital, Birmingham, 29.
Department of Pathology, Royal Infirmary, Worcester.

Despatch instructions.—To comply with the inland postal regulations, specimens of blood must be sent by letter post—*not* parcel post or sample post—packed in the manner described below, and conspicuously marked FRAGILE WITH CARE and bearing the words PATHOLOGICAL SPECIMEN (AGRICULTURAL POISON). A note should accompany each specimen giving (*a*) the name and age of the patient; (*b*) an indication of the degree of exposure to the poison, naming it if possible; and (*c*) details of any symptoms which may be referable to such exposure. Specimens must be enclosed in a receptable, hermetically sealed or otherwise securely closed, and this receptacle must itself be placed in a strong wooden or metal case (or other case which has been approved by the Post Office) in such a way that it cannot shift about, and with a sufficient quantity of some absorbent material (such as sawdust or cotton wool) so packed about the receptacle as absolutely to prevent any possible leakage from the package in the event of damage to the receptacle.

NATIONAL HEALTH SERVICE IN 1959

THE Mental Health Act of 1959 figures prominently in the Ministry of Health's report for last year on the National Health Service.[1] In his introduction, Mr. Derek Walker-Smith, the Minister of Health, declares: "This Act adds a notable chapter to the story of social progress, and completes the movement towards integration of all services centring on health which was begun with the National Health Service Act, 1946."

Finance

The total cost of the National Health Service in England and Wales in the financial year ended March 31, 1959, was about £671 million—£45 million more than that in the previous year. The cost of the hospital and specialist services went up by £26 million. As a result of the increased income from contributions after the passing of the National Health Service Contributions Act, 1957, the percentage of the total cost borne by the Exchequer fell from 80 in 1956–57 to 76·6 in 1957–58; and in 1958–59 the percentage fell further to 72·4 owing to the further increase in contributions following the passing of the National Health Service Contributions Act, 1958.

Volume of Hospital Work

About 4 million courses of inpatient treatment were completed in 1959—an increase of 3·0% over the number in 1958. This increase was achieved even though during

1. Report of the Ministry of Health for the year ended Dec. 31, 1959. Part 1: (1) The National Health Service; (2) Welfare, Food and Drugs, Civil Defence. Cmnd 1086. H.M. Stationery Office. Pp. 281. 13*s*.

the year the number of available beds fell slightly (by 1500) to 475,000. On the other hand, those awaiting admission at the end of the year—totalling 476,000—were 13,000 more than at the end of the previous year.

Mental Hospitals

The number of patients in designated mental hospitals continued to decline—from 138,122 at the end of 1958 to 133,154 at the end of last year. This decline, which began in 1954, is partly due to the " de-designation " in that year of beds for the reception of patients outside the Lunacy and Mental Treatment Acts; " but there is no doubt that it does reflect a steady real decline in the number of patients." In the long run there is likely to be a notable decline in the need for long-stay accommodation in psychiatric hospitals both for mentally ill and for mentally subnormal patients. Such a decline should in the first place make it possible to relieve overcrowding.

" But it is clear that, in long-term planning, it is now necessary to begin seriously to allow for the fact that we are likely in future not to need nearly so many beds as are now being used for long-stay patients suffering from mental illness. It will no doubt be possible to use some of them for different purposes—for example, caring for patients suffering from other types of chronic illness, as has already been done at one hospital in the north of England. Others will probably have to be dispensed with altogether because they are in unsatisfactory accommodation which, perhaps because of remoteness or the inordinate size of the hospital, is not worth reconditioning or converting. Clearly, therefore, during the next few years much careful thought will be needed before any large-scale new developments for long-stay patients in mental hospitals are embarked on. Similarly, difficult problems arise when major works of renewal or up-grading are being considered at existing mental hospitals, so as to avoid the danger of spending a lot of money on a hospital which in 10 or 15 years may be partly or wholly out of use or being put to some quite different purpose, and yet to provide all the amenities needed by existing patients."

General Practice

Of all principals in general practice the proportion in partnerships increased from 67·0% in 1957 to 67·6% in 1958 and to 68·9% in 1959. The average number of persons on a doctor's list increased from 2267 at July, 1958, to 2282 at July, 1959.

General Dental Service

The number of dentists in the Service at the end of 1959 was 10,418, of whom 517 were women. This represents an increase of 144 over the total at the start of the year. The number of students engaged in the first year of the professional course in the 1959–60 session at dental schools in England and Scotland was 622, compared with 652 in the previous year. Schemes are in hand for increasing the number of places in dental schools.

Pharmaceutical Service

During the year pharmacists and other suppliers dispensed 214,029,087 prescriptions at a total cost of £72,908,155. The average cost per prescription was 6 shillings 9·76 pence. The increase of about 10,700,000 in the number of prescriptions over the total for 1958 was mostly accounted for by the influenza epidemic which began in February, 1959. The increase by over £7 million in the total cost was due both to the increased number of prescriptions and to the higher cost per prescription; this cost was 4½*d.* more than in 1958. " Since there has been no change in chemists' remuneration during the year and no evidence that quantities prescribed were larger than in 1958, it seems that the increase of 4½*d.* must be largely attributable to the greater cost of the drugs supplied."

In England Now

A Running Commentary by Peripatetic Correspondents

I WAS reading the *Senior Registrar's Post and Greybeard's Gazette* when the phone rang to summon me to my chief, back after a long absence. " You'll find a great change in him," said his secretary, but I was hardly prepared to see a Yeti sitting at his desk, covered in natty red fur and wearing spats and a carnation—it was a chilly morning. " Ah, Carruthers," he said, in good English but with a strong Central Nepalese accent, " I think I've got away with it with Miss Watson, though she looks at me a little queerly sometimes, but it is no use trying to conceal from *you* that I'm not Dr. Brown." Dr. Brown, I should explain, had remained at his desk oblivious to the passing years, long after the customary age of retirement and, when drawing-pins stuck to the seat of his chair with ' Plasticine ' had failed to make their point, we had started on the well-known parkinsonian treatment of a course of intensive foreign travel. After trial runs to a conference on St. Anthony's fire at Padua and the wame-ill at Pitlochry, we sent him to a study-group on the polarity of polarimeters at Spitzbergen and then hurried him off to a seminar on monocular chlorosis in Little Yellow Gods at Khatmandu, since when we had had no news. " I met him in the foothills," said the Yeti, " and found he had been converted to Buddhism and the contemplative life—*om mani pudmi hum*, and all that. He is quite well and happy, making paper prayer-wheels out of the seminar documents. Besides, between you and me, he has met Miss Prout—you remember, the governess whose elastic-sided boots were responsible for the first photographs of Yeti tracks [1]—and he's thinking of settling down out there." " And you Sir," I stammered, " are you . . . have they . . . ?" " Oh my position is all open and above-Board," he broke in. " I wanted to broaden my experience, and the conversation of Sherpas gets a bit monotonous, in spite of occasional Hillarity. But "—here he scowled hideously—" the R.H.B. wouldn't make me a consultant. Of course the post is graded as a consultant post so I shall get the allowance. And after all "—he brightened up—" I am probably the only Abominable SHMOman in the Service!" With a laugh like an avalanche ringing in my ears, I left the room and went back to my own part of the lab.

* * *

Among the jostling Philistines there were undoubtedly a few genuine apostles: though it's hard to tell these days, when all the catch-phrases can be so easily picked up from the reviews. For my own part, I reflected sadly as I walked around the exhibition, there was clearly some central synaptic inhibition interfering with my perception of the works of the greatest painter of our age. And then, suddenly, tucked away in a corner, I saw a picture I understood. The title in the catalogue was immaterial: it may have been a woman in a red arm-chair to some people, but I knew better. There was no mistaking it: it was a very nice interpretation of the lateral ventricles of the brain, and there, at the top of the picture, was a beautiful optic chiasma. True, the chiasma was in an unusual position, but all great painters have the right to alter spatial relations if they think fit.

After that it was easy. Traces of an anæsthetist's nightmare were discernible in one of the cubist paintings, with the elephant tubing and the ' Fluotec ' vaporiser irretrievably disconnected; normal and abnormal histology abounded everywhere; and one whole wall was seemingly given to my old embryology lecturer, vainly trying, with the aid of a couple of dusters, to imitate the behaviour of the rotating gut.

I felt better: in the space of a brief hour or so modern art had become comprehensible after all.

* * *

The hospital where I was recently warded for an operation has a bevy of cadet nurses. At their age, they are merged into a composite charm of clear eyes, delicate complexions, and

1. *Lancet*, 1951, ii, 1179.

youthful suppleness. One girl, however, was readily distinguishable by her abundant mop of auburn hair which cascaded shoulder-length. One morning she came on duty with her head lamentably shorn—short and ragged, the work of another cadet. Matron had said it was too long, she told me when I commiserated. "And so it had to come off. Of course, I didn't have the money for a proper cut so late in the month." Her tone held no resentment. Matrons and nurses' pay were formidable facts; but youth has plenty of time to recover its losses and regrow its shorn tresses.

"Decadent nusses, I thought they wuz called!" remarked an old fellow patient. I sympathised with his misunderstanding when another sweet young thing, asked whether she had gone to watch That Wedding on her day off, replied that she wouldn't cross the road to see any wedding. Getting married, she declared, was a mug's game. "Catch me settling down with one person," she exclaimed, "I like a gay life." Further questioning revealed that she had no particular boy friend. Medical students, in her opinion, were "soppy", and the housemen "too stuck up for words." Her favourite recreations were going dancing with some of her friends and taking her young brother to rugger matches. He wasn't all that keen on cricket, but she was hoping to take him to see the South Africans at Lord's.

• • •

In this country the after-dinner speech is a hazard to be faced with equanimity or otherwise, and A. P. Herbert has inveighed against the necessity to make one. ("I will not make a speech to-night, my neighbour's eyes are very bright"). But a few weeks ago I was privileged to attend a public dinner in the South of France and to learn about French custom in this respect.

We settled ourselves at table at 8 P.M., studied the elaborate menu, and prepared for the Lucullan repast. The waiters and waitresses, the latter in attractive Provençal costume, stood poised in the wings. But first, Monsieur le Président rose to say some graceful words of welcome to the guests, and particularly to those like ourselves, from foreign parts. He spoke for about 20 minutes and was loudly applauded. Good; now for *les tarraietos aux senteurs de Provence*. No, the president called on another speaker to say a few words, and further graceful and polite things were said for another 20 minutes. By then we were hungry and quite prepared for the *tarraietos*, which I didn't recognise under that name. There was another postponement of the voyage of gastronomic discovery while a third speaker, very properly, praised the chief organiser of the conference for his magnificent spade-work and we were treated to 15 minutes of delightful French. I noticed my neighbour on my left looking at his watch, and I turned and whispered that in England we usually have the speeches after dinner. He replied with a hint of firmness in his voice: "In France we have them both *before* and *after* dinner, and I have to catch my train back to Paris at 10 P.M." There was a fourth speaker and the waiters and waitresses were galvanised into activity at exactly 9.10 P.M. The professor from Paris hurriedly ate the first course, which turned out to be a delicious pâté, drank a glass of *vin de Cassis du Château de Fontcreuse*, and departed. The banquet was worth waiting for, and during its course we were treated to some traditional Provençal songs and dances, accompanied by a pipe and tambour band. The young girl dancers weaved in and out between the tables while the meal was being served and looked very jolly and fresh. At 11.10 P.M. the after-dinner speeches began but few of the guests were really in the mood to listen attentively. The evening ended with more dancing on the terrace outside the old palace where the banquet had been held, and we all joined hands and danced la Farandole under the Mediterranean new moon. They order these things very well in France, and particularly in Provence.

• • •

Overheard at our local clinical meeting.

Neurosurgeon: "Who is showing that hysterical paraplegia? I did a laminectomy on him years ago."

Letters to the Editor

POLIOMYELITIS IN THE VACCINATED

SIR,—We have read with interest the communication by Dr. Geffen and Dr. Spicer (July 9), which is reassuring in its evidence of continued efficacy and safety of poliomyelitis vaccine used in this country. It would be interesting to know how many of the 137 cases notified on clinical grounds as paralytic poliomyelitis in vaccinated persons were actually due to infection with poliovirus.

It is increasingly evident that acute anterior poliomyelitis is a clinicopathological syndrome of multiple ætiology, of which polioviruses have been the commonest cause. As poliovaccination becomes more complete, the number and proportion of paralytic cases due to poliovirus infections will diminish. Other enteroviruses will thus become more prominent as causes of paralytic disease, particularly since the same alterations in our way of life which changed poliomyelitis from endemic "infantile paralysis" into an epidemic paralysing disease of older age-groups must surely be affecting the equilibrium between the human population and other enteroviruses.

That this is not merely a theoretical possibility is evidenced by the increasing frequency of reports of outbreaks of aseptic meningitis and other diseases due to non-polio enteroviruses and of cases of paralytic and fatal disease due to Coxsackie or Echo viruses. In Scotland in 1959 poliovirus made a negligible contribution to serious disease.[1] Studies in this laboratory, to be published, showed that Coxsackie A7 virus was the main identified cause of paralytic poliomyelitis, and that the major cause of aseptic meningitis was a virus, not previously recognised in this area, which appears to be an enterovirus but not to belong to the known groups of poliovirus, Coxsackie, or Echo types 1 to 27. These findings apply to the Western and Eastern Hospital Board regions of Scotland, an area which includes the large populations of the Clyde valley and Dundee. Data in press [2] describe our investigations of cases notified as poliomyelitis in vaccinated persons during 1959. Poliovirus was isolated from only one such patient—who proved, on investigation, to be unvaccinated. Other enteroviruses were isolated from 7 cases, and the single death was associated with Coxsackie A7 virus infection.

This important problem demands continuing scrutiny. The necessary laboratory facilities are now generally available, and it is to be hoped that every case of paralytic poliomyelitis in a previously vaccinated person will be investigated virologically.

University Departments of Virology and Bacteriology, Ruchill Hospital, Glasgow.

N. R. GRIST
I. B. R. DUNCAN.

THE FEMALE PROSTATE

SIR,—Mr. W. Skyrme Rees (July 9) suggests that the glands round the female urethra are not the homologue of the prostate in the male. In my article of June 18 and in a previous communication [3] I stressed that the histology of the material removed in my cases had never simulated true prostatic adenoma and I detailed the changes I had found. The exact nature of the changes at the bladder neck are not really of very great importance. What is of importance is that these changes give rise to a type of urinary obstruction which clinically simulates prostatic obstruction.

1. Grist, N. R. *Brit. med. J.* 1960, **i**, 344.
2. Grist, N. R., Duncan, I. B. R. *Hlth Bull., Edinb.* (in the press.)
3. Moore, T. *Proc. R. Soc. Med.* 1953, **46**, 558.

It should be remembered that the signs of prostatism in the male are not always associated with a typical adenomatous enlargement of the gland; some are examples of "prostatism sans prostate" in which inflammatory or glandular bars or fibrous contractions at the bladder neck are responsible. Most doctors not especially trained in urology regard all such cases as suffering from "enlarged prostates". In order, therefore, to stress that exactly similar syndromes occur in the female, I entitled my article The Female Prostate. My object was to make the syndrome better known, particularly to family doctors. One may also mention here that similar changes occur in children and infants of both sexes and cause urinary obstruction, often with serious consequences.

In support of his assertion that no prostatic homologue occurs in the female he states that carcinoma of the prostate has never occurred in that sex. In view of the high œstrogenic environment in which it would have to exist perhaps this is not surprising!

Mr. Skyrme Rees states he treats such cases by regular intermittent dilatation with good results and suggests that the value of my transurethral resection is in the associated urethral dilatation. The fact that in my cases only one urethral dilatation (and bladder-neck resection) was necessary surely entirely refutes this suggestion. The cases he is describing must be of a different type. Those I have reported were suffering from definite bladder-neck obstruction with residual urine and were just as definite as prostatic obstruction in the male; no amount of urethral dilatation per se would cure them. As mentioned in my paper there are cases where a narrowing of the urethra, sometimes following colporrhaphy, is the obstructive factor, and these cases can be cured, of course, by regular urethral dilatation. It is also well known that many women who complain of recurrent attacks of frequency of micturition and dysuria suffer from chronic inflammatory changes in the urethra and can often be miraculously relieved by urethral dilatation. Possibly Mr. Skyrme Rees is confusing these types with the female prostate syndrome. I am very grateful to him, however, for raising these interesting points and for his kind remarks on my work.

Manchester. THOMAS MOORE.

TOO MANY CALORIES

SIR,—Dr. Ross (July 9) quite rightly asks "Did the results last?", and suggests that we should inquire into the long-term results of treatment of obesity. Despite the enormous numbers of papers on the management of overweight, there has been little published on the eventual results. One such paper,[1] by Dr. Mullins, reported an investigation of cases seen by me up to eight years previously and compares results with those achieved by more recently developed methods. These are relatively small groups of patients (61 and 40), but since then a very much larger series has been collected and a ten-year follow-up is being made.

This is not the place for a detailed report, but it appears from our research so far that satisfactory weight-loss can be achieved in over 70% of cases without inflicting too much misery on the patients. Usually the relief of symptoms which have been aggravated by the overweight more than compensates for the deprivation of comfort and pleasure that eating has afforded. The results are likely to be lasting if supervision is continued until normal weight is achieved. Drug therapy and methylcellulose bulk are, in my opinion, of little value; a very large proportion of over 1000 patients studied in my clinic have taken various appetite-reducing drugs without benefit and often with unpleasant side-effects. Rapid weight-loss is much more likely to be accompanied by untoward symptoms, and a desirable rate of loss is about 1 lb. per week, even though ideal weight is not reached for eighteen months or more.

1. *Med. Pr.* 1958, **239**, 126.

It is useless to present an obese patient with a supply of appetite-reducing drugs and a printed sheet of dietetic instructions. These patients require personal advice and instruction; they need symptomatic treatment for their varied symptoms, and very often they need some sort of psychotherapy or "therapeutic counselling".

St. James' Hospital,
London, S.W.12. A. KAHAN.

RELIEF OF PAIN IN RESPIRATORY FAILURE

SIR,—Recently Dr. Judge and his colleagues (June 25) suggested that 'Pethilorfan' might be a "desirable substitute" for pethidine alone in the treatment of pain in patients with severe respiratory disease. This proprietary mixture contains pethidine and levallorphan—the latter is presumably included as an antagonist to the respiratory depressant action of pethidine. It seems to me that this letter and the results quoted in it are open to misinterpretation.

There are certain criteria which must be satisfied when assessing whether a drug or mixture of drugs cause respiratory depression. These are well enunciated in one of the papers,[1] quoted by your correspondents. If I interpret these principles correctly they are:

(1) Depression of the respiratory centre cannot be readily detected by simple measurements of respiratory rate, depth, or minute volume. Such measurements on normal subjects after morphine showed no significant effect of this drug.[1] However, when alveolar pCO_2 was measured simultaneously a rise in CO_2 tension was observed after morphine.[1] This indicates that during the breathing of air alveolar (or arterial) pCO_2 is a more sensitive indicator of respiratory depression than respiratory volume.

(2) By "driving" the respiratory centre with increased concentrations of inspired CO_2 the ability to detect drug depression is improved.[1] The most sensitive index of central respiratory depressant effects of drugs appears to be a comparison of the ventilatory responses to the same level of increased alveolar pCO_2. This may be done by extrapolation on a CO_2 sensitivity curve [1] or by holding end-tidal pCO_2 constant by varying the inspired CO_2 concentration.[2] The latter method is especially useful in detecting depression of a minor degree.[3]

None of these criteria have been satisfied in the results quoted by your correspondents. CO_2 content cannot be really considered a sensitive enough indicator of respiratory depression: pCO_2 (and probably pO_2) are the variables that count. Thus, your correspondents have not shown, as they claim, that the respiratory depression known to follow the use of pethidine did not occur.

In addition, there have been two excellent papers indicating that levallorphan mixed with the opiate derivative levorphan does not abolish the respiratory depressive activity of the latter drug.[4 5] Thus it is unlikely that there would be any advantage in having a mixture of morphine and levallorphan. These results, however, cannot necessarily be applied to the unrelated drug pethidine.

Presumably Dr. Judge and his colleagues justify their contention that pethilorfan is safe on the basis that their subjects were patients with impaired pulmonary gas exchange. But it is difficult from their quoted results to assess the degree of impairment. The mean levels of oxygen content *suggest* that their patients may have been desaturated, but had any of the patients a raised pCO_2? Anyhow, the response of patients with respiratory impairment to such drugs as pethidine is very variable and one would want to see the results from a larger series

1. Loeschke, H. H., Sweel, A., Kough, R. H., Lambertsen, C. J. *J. Pharmacol.* 1953, **108**, 376.
2. Lambertsen, C. J., Wendel, H. *J. appl. Physiol.* 1960, **15**, 43.
3. Semple, S. J. G., Fidler, J. P., Lambertsen, C. J. *Fed. Proc.* 1958, **17**, 1621.
4. Thomas, D. V., Tenney, S. M. *J. Pharmacol.* 1955, **113**, 250.
5. Eckenhoff, J. E., Hebrich, M., Hedge, M. J. D., Jones, R. E. *ibid.* 1950, p. 332.

before any idea of the safety of pethilorfan could be assessed in these circumstances.

Their results, however, are certainly of interest and one must hope they will give further information so that an objective assessment can be made.

Department of Medicine,
St. Thomas's Hospital, S.E.1. S. J. G. SEMPLE.

ANTICOAGULANT DRUGS IN THE TREATMENT OF PULMONARY EMBOLISM

SIR,—In 1947 Jorpes,[1] concluding his survey of the extensive Swedish experience of anticoagulants in venous thrombosis and pulmonary embolism wrote: "The results in using anticoagulant therapy are therefore as striking as any hitherto reported following the introduction of a specific therapy in medicine." The convincing mass of evidence behind this statement included 166 cases of sudden but not immediately fatal pulmonary embolism, without other signs of thrombosis: of these, 63 were treated conservatively and 21 died; 103 were treated with anticoagulants and none died. Soon afterwards the judgment of Jorpes was abundantly confirmed by many critical studies in the treatment and prophylaxis of thromboembolism. This evidence seemed decisive enough to make reasonable the view that in this condition neglect of anticoagulant treatment was neglect of the patient.

It is therefore startling to find that in 1960 a strictly controlled trial of the kind reported by Dr. Barritt and Dr. Jordan (June 18) should be thought either necessary or justifiable. Among the arguments given in its justification is the one that untreated series previously reported include patients dying suddenly from embolism before treatment is possible, whereas the treated series obviously do not include such cases. This is simply not true of some of the earlier reports: Jorpes,[1] for instance, was careful to exclude such cases from his untreated series. Another of the authors' arguments is based on the conclusions of Marks et al. (1954),[2] allegedly giving "support for scepticism of the protection afforded by anticoagulants". But these conclusions have surely been misunderstood by Dr. Barritt and Dr. Jordan. Marks and his colleagues found that, in spite of early treatment of deep-vein thrombosis once diagnosed, deaths continued to occur suddenly—in *other* patients—from massive pulmonary embolism. They wrote: "It must be emphasised again that these fatalities took place in patients who gave neither symptoms nor signs of leg-vein thrombosis and therefore had received no treatment with anticoagulants." Whether or not such patients would be protected by *prophylactic* anticoagulant treatment was a question not asked by Marks et al.,[2] but it has been answered in the affirmative by several studies, notably those of Wise et al.[3] and Sevitt and Gallagher.[4] In the 1135 cases of venous thrombosis treated by Marks et al. over a period of five years there were only 3 deaths.

Goodman and Gilman,[5] commenting on the very great reduction in morbidity and mortality from thromboembolism in surgical patients and the almost negligible risk of hæmorrhage, write: "It is abundantly clear that death from thrombo-embolism in patients not given anticoagulants is a far greater hazard than death from hæmorrhage in those treated with the drugs."

1. Jorpes, J. E. *Surg. Gynec. Obstet.* 1947, **84**, 677.
2. Marks, J., Truscott, B. M., Withycomb, J. F. R. *Lancet*, 1954, ii, 787.
3. Wise, W. D., Loker, F. F., Brambel, C. E. *Surg. Gynec. Obstet.* 1949, **88**, 486.
4. Sevitt, S., Gallagher, N. G. *Lancet*, 1959, ii, 981.
5. Goodman, L. S., Gilman, A. The Pharmacological Basis of Therapeutics. New York, 1956.

In these days when chemical remedies, potent for good or ill, are multiplying so rapidly we should be the last to underestimate the need, where reasonable doubt exists, for early and rigorous clinical trials using concurrent series of patients allocated by chance to treatment and control groups. But the important conditions for such a trial are that the benefit conferred by the drug, in relation to its toxic effects, should be genuinely in doubt, and that the trial should take place early, before an accumulation of presumptive or indirect evidence in favour of the drug makes it more and more difficult, on ethical grounds, to withhold it from half of the patients. In the case of pulmonary embolism, with all due regard for the difficulties in its diagnosis, we believe that the evidence available many years ago put the issue beyond all reasonable doubt.

The cause of the controlled clinical trial is a good one, in season, but we fear it may be damaged by such intemperate enthusiasm for it as has been shown in this instance by Dr. Barritt and Dr. Jordan. We feel that this is the more important since the instance is not an isolated one but illustrates an increasing trend in the medical literature.

Department of Pharmacology and Therapeutics,
Queen's College, Dundee. R. B. HUNTER
W. WALKER.

GRAM-NEGATIVE BACTERIÆMIA WITH SUDDEN HYPOTENSION

SIR,—The interesting article by Mr. Aldridge (July 9) reminds me of an article [1] by Dr. Geoffrey V. Balmforth on excessive ganglion blockade precipitated by chemotherapy. He found that the effect of ganglion-blocking drugs can be enhanced by antibiotics in patients with pyelonephritis. I wonder whether there might be a common explanation for these observations.

Hillerød,
Denmark. TORBEN ANDERSEN.

BACK PAIN AND HYPERÆSTHESIA

SIR,—Dr. Cyriax has once more attacked the use of the word osteopathy.

Here is a subject of enormous importance—back-pain and manipulation—which needs to be far more widely discussed and studied. Clinically there is no doubt that there is a lesion of the intervertebral joints which causes disabling symptoms and which can be treated quite simply. Dr. Glover refers to it in discussing the back-pain syndrome in his article of May 28. Dalgleish [2] calls it the dysarthric lesion, the osteopath calls it the osteopathic lesion, and so on. There is no hurry in agreeing on a name; it does not matter what it is called so long as it is recognised as a clinico-pathological entity.

There is scarcely any doubt that manipulation is the best single way of treating these lesions; and that it should be applied specifically in a way that needs precise diagnosis and technique. The fact that this is practised successfully by osteopaths more than by medical men is of no consequence. What the medical profession has to do is to learn what is practical and useful about it.

Dr. Cyriax refers to "the part played by the intervertebral disc in causing fixation of one vertebra on another by internal derangement, with consequent pain . . ." which has no real evidence to support it; and he refers to his contention that manipulation is a means for reducing "slipped discs", which ignores the evidence that discs do not slip unless they are degenerated and therefore irreducible.[3]

1. *Lancet*, 1959, i, 707.
2. Dalgleish, P. H. *Mediese Bydraes*, 1959, **5**, no. 24.
3. Hendry, N. G. C. *J. Bone Jt Surg.* 1958, **40B**, 132.

Specific joint manipulation is a most useful skill, but whatever else it may do it does not reduce a nucleus pulposus which has herniated through a degenerated annulus fibrosus. What it does do is clinically objective, but it needs a tremendous amount more study.

Aberdeen. DUNCAN TROUP.

CONVERSION OF GENERAL WARDS INTO PRIVATE WARDS

SIR,—In many hospitals the traditional ward, with its double row of beds and complete lack of privacy, is clear evidence of past standards and attitudes to patients. Mr. Vaughan Hudson, in his imaginative article (July 9), reminds us that the hospital today should cater for all sections of the community and that the modern patient is not so inclined to accept the numerous auditory and visual assaults inflicted by an open ward.

I am sure, however, that he is wrong in suggesting that the whole ward should be converted to single rooms. A surprising number of patients feel acutely miserable and uncomfortable in a room by themselves and are much happier in the company of others. Some people, left to their own devices in a single room, are inclined to be introspective and full of self-pity. Their recovery is probably hastened by contact with other patients. There is much to applaud in Mr. Hudson's arrangement, but I think it would be wiser and more realistic to have one 4-bedded and a few 2-bedded rooms on his ward. Sister is usually very good at deciding which patients should go where.

With single rooms and a panel system of lights for summoning a nurse (as described by Mr. Hudson) there is always the possibility, particularly in a surgical ward, that a patient in difficulties may not be able to attract attention. Much better would be a slightly raised nursing station with suitably placed glass windows so that the nurse on duty could see not only down the central corridor but also into each room.

Department of Midwifery and Gynæcology,
Royal Victoria Infirmary,
Newcastle upon Tyne. J. K. RUSSELL.

ORNITHOSIS AND THE RAILWAY GUARDS

SIR,—I direct the attention of Mr. Osman (July 16) to the report [1] of a recent outbreak of ornithosis in Glasgow involving two pigeon-fanciers and their flock. Serological tests at this laboratory established the diagnosis in the two cases and in their sick and apparently healthy birds. Ornithosis virus was isolated from the birds.

The general risk should not be exaggerated: over the past 11 years, our investigations have showed serological evidence of ornithosis in only 19 patients, of whom 2, aged 62 and, 75 years, died. None of these was a railway guard. No contact with birds was traceable in 12 cases, and apart from the 2 pigeon-fanciers I have mentioned only doubtful contact was recorded with budgerigars (3 cases), a sick canary (1), and wild pigeons nesting on the windowsill (1). Of 14 pigeon-fanciers investigated in 1950, only 1 showed a low and probably insignificant titre of antibodies. Both by isolation of the virus and by serological tests ornithosis infection was found in the wild pigeons of Glasgow, as has been reported in many cities of this and other countries. No evidence of infection was found in 12 starlings.

My own view is that ornithosis infection in Glasgow is usually acquired from wild pigeons. The chance of effectively intimate contact with an infective pigeon-dropping is small, and human cases of the disease are correspondingly few. Human disease caused by ornithosis strains derived from pigeons is less severe than the dangerous infections acquired from parrots and budgerigars.

I thank my colleagues in the Public Health Department of Glasgow, Greenock, and Renfrewshire for assistance in tracing sources of infection in these cases.

University Department of Virology,
Ruchill Hospital, Glasgow. N. R GRIST.

1. Grant, W. *State vet. J.* 1960, 15, 70.

SIR,—In the *British Medical Journal* of July 26, 1952, p. 189, there appeared an article entitled Psittacosis in a Family by Dr. C. M. Miller and myself, in which we reported this condition in a father and his son who had handled domestic pigeons. In it Mr. Osman will find the proof he seeks of pigeons as the source of the infection.

Perhaps it would have been more accurate to have entitled our paper Ornithosis rather than Psittacosis. Had we done so it might not have been overlooked by your recent correspondents.

Liverpool. B. K. ELLENBOGEN.

TREATMENT OF OBESITY BY INTESTINAL OPERATION

SIR,—Severe obesity in individuals without the force of character to adhere to long and trying dietetic measures is an intractable and not uncommon condition. Attempts to help such patients surgically have hitherto been restricted to mechanical removal of superficial adipose tissue, a difficult treatment which can be of value only in comparatively rare cases. A more physiological way is to attack the absorptive power of the organism by surgical means, a theoretically sound approach, but this seems never to have been tried. At least such trials are unknown to me, and E. H. Rynearson and C. F. Gastineau do not mention this possibility in their book *Obesity*.

With the efficiency of modern surgical technique and its low operative mortality it seems worth trying to reduce the energy absorptive capacity of the organism by means of intestinal surgery in selected cases. As the main site of the absorption of energy-producing nutrients is the jejunum, the simplest approach would be resection of a suitable portion of this part of the small intestine, beginning somewhere below the ampulla of Vater, and making an end-to-end anastomosis. This would not be very complicated, and the only difficulty apparently is to decide how large a part of the jejunum it is suitable to remove. If too little is resected the effect on the absorptive capacity may be too small to combat the obesity, and if too much is resected progressive intractable emaciation may result. In each case it is necessary to reduce the absorptive capacity sufficiently to curtail the energy absorption (on a diet the patient is able to adhere to indefinitely) to well below his daily energy requirement.

This brings us to a difficulty, for if treatment is successful it seems likely that weight-loss will continue after the normal weight has been reached. Only if the reduced absorptive capacity obtained is sufficient to maintain the normal weight of the patient, because the weight loss has been followed by reduced energy requirement, can one hope to reach equilibrium on the patient's normal weight and a diet to which he can adhere.

Intestinal resection is not therefore very attractive, and it would be better and less traumatic to use a by-pass operation where part of the jejunum below the ampulla of Vater was transformed into a cul-de-sac not traversed by food. With such an operation it would be possible to raise the absorptive capacity later by reoperation if necessary. It has the drawback that pernicious anæmia may follow; but this could easily be mastered by hæmatological control and adequate treatment. If other difficulties, such as ileus or severe dyspepsia, should develop as a sequel to such jejunal cul-de-sacs, one might as an alternative operation remove part of

the jejunum from the intestinal canal without resection, performing a temporary or permanent displacement with both ends of the removed part of the intestine placed as cutaneous fistulas. Later a resection might follow when a suitable equilibrium had been arrived at.

Before such operations are performed in man, experimental studies must be made on animals—e.g., rats made obese by means of controlled forced feeding. Data could also be obtained on obese as well as normal-weight persons from whom large parts of the small intestine have been removed.

Svendborg, Denmark. TORBEN K. WITH.

DISPOSABLE UNDERPADS FOR INCONTINENT PATIENTS NURSED AT HOME

SIR,—

"Laundry services are of great value where disabled and bedridden patients are concerned. If a patient is regularly incontinent the strain of providing clean linen and blankets is often more than the average family can bear, but when there is a possibility of the Local Authority doing this heavy wash many more families are prepared to look after an incontinent or partly incontinent relative."—Lord AMULREE.[1]

Nursing the incontinent patient at home is a severe strain on the family and on the nurse. It has often been reported that many families who have cared for aged bedridden relatives request hospital admission once the patient becomes incontinent, because of the difficulties of providing adequate clean bed linen. Boucher [2] found that many patients were admitted solely for reasons of incontinence, and this has been confirmed by several general practitioners, in this county.

It is hard to assess the frequency of incontinence in the aged nursed at home, but a survey in Nottingham indicated that 2·1% of old people visited by a district nurse or home-help were incontinent. This estimate may well be on the low side but even accepting the figure it means that in this county (population 147,000) at any one time there are approximately 100 aged persons being nursed at home who are incontinent; some doubly incontinent. Incontinence in the aged may be due to many factors—disease, mental confusion, or simply difficulty of access to toilet. Even when the remedial factors have been attended to, and they should be in every case, there still remain many cases where incontinence remains a major problem in home nursing.

In 1959 a county conference was arranged between general practitioners, consultant geriatrician, county welfare officer, and the health department to discuss various problems relating to the care of the aged. One matter raised by the general practitioners was the question of a domiciliary laundry service for the aged incontinent patients. This matter was gone into very thoroughly but it presents many difficulties in a county which is partly rural and partly industrialised. Commercial laundries were not willing to do this work, and providing a county laundry service purely for this type of work would prove costly, particularly as regards collection and distribution of linen.

One solution seemed to be the use of disposable underpads and in 1959 a small supply of underpads was obtained for trial. These disposable underpads are made of soft non-woven fabric containing many layers of absorbent paper tissue. (The size used is 30 × 23 in. with a polyethylene-coated paper back.) The polyethylene back prevents moisture penetrating to the bed, and the underpads are made with a seepage-resistant fold on each side of the pad, again to prevent moisture damaging the bedding and the transverse bonding of the absorbent paper helps to prevent breakdown of the pad when it is saturated.

Underpads are purchased in bulk and supplies made available to each district nurse, who leaves a small number of underpads in the homes of incontinent patients. The district nurse instructs the relatives or family how to change pads after saturation and on the number of pads to use per day. The average patient uses approximately four pads per twenty-four hours but there are considerable variations. After use, the underpads are burnt either in a garden incinerator or on an open fire and this does not cause any offence or difficulty.

In practice the underpads are effective and comfortable and do not disintegrate with wetting. In a county such as this, partly rural and partly industrialised, underpads cost no more than the purchase of a small supply of linen and the provision of domiciliary laundry services. Underpads are much more convenient to use, and a complete cover for the whole county can be given with much less trouble than a domiciliary laundry service. The underpads do effectively prevent soiling of bedding and enable many incontinent patients to remain at home.

The underpads described above are obtained from Johnson & Johnson, Slough, and cost approximately 8*d.* each, purchased in bulk. We have no accurate cost of providing clean linen at home, but figures given by a city where a domiciliary laundry service for incontinent patients has been established were 7*d.* per sheet. In a county this unit cost per sheet would be higher due to the increased collection and delivery charges. Although the cost of the underpads seems high they serve approximately the same function as a domiciliary laundry service, and in a county area the cost does not seem to be any greater than the provision of a domiciliary laundry service—in fact, it may be less.

Mold, Flintshire. G. W. ROBERTS
L. MANN.

ATROPINE IN MONGOLS

SIR,—After reading the article by Berg et al.[1] we also became interested in investigating the response of mongols to atropine. In our institution for the retarded there are over 200 mongols. It has not been our experience that these mongols show unusual sensitivity to atropine although this drug has been used here for some years, particularly as a pre-anæsthetic medication. We have not observed gross E.E.G. changes or changes in sensorium, pulse-rate, or respiratory rate.

TABLE I—PUPILLARY DILATION (IN MM.) CAUSED BY ATROPINE SULPHATE AND OBSERVED AT VARIOUS INTERVALS

Time interval	30 mongols		30 non-mongols		P (Student's "t")
	Total dilatation	Mean dilatation	Total dilatation	Mean dilatation	
15 minutes ..	101·0	3·4	55·5	1·9	<0·001
1 day ..	136·0	4·5	111·0	3·7	<0·005
2 days ..	130·0	4·3	106·0	3·5	<0.005
3 days ..	118·0	3·9	94·0	3·1	<0·005
6 days ..	77·5	2·6	39·0	1·3	<0·001

TABLE II—PUPILLARY DILATATION (IN MM.) CAUSED BY HYDROXYAMPHETAMINE HYDROBROMIDE AND OBSERVED AT VARIOUS INTERVALS

Time interval	30 mongols		30 non-mongols		P (Student's "t")
	Total dilatation	Mean dilatation	Total dilatation	Mean dilatation	
10 minutes ..	8·5	0·3	1·5	0·05	<0·01
20 minutes ..	36·5	1·2	14·5	0·5	<0·001
30 minutes ..	69·5	2·3	36·0	1·2	<0·001
1 hour ..	93·0	3·1	55·0	1·8	<0·001
2 hours ..	75·5	2·5	42·0	1·4	<0·001
3 hours ..	62·0	2·1	27·0	0·9	<0·001
4 hours ..	45·0	1·5	13·0	0·4	<0·001
6 hours ..	16·5	0·5	3·0	0·1	<0·025

A total of 60 patients were selected, 30 mongols and 30 non-mongols. Each mongol was paired with a non-mongol control in regard to age, approximate intelligence, eye colour, and sex. The age-range was 12–26 years, and the eye-colour range was light "blue" to dark "brown". For each patient 1% atropine sulphate (a parasympatholytic pupillary dilator and cycloplegic) was instilled into one eye, and the two eyes were observed by daylight at various time-intervals. One month later 1% hydroxyamphetamine hydrobromide (a sympathomimetic

1. Amulree, Lord, *Publ. Hlth*, 1957, **72**, 202.
2. Boucher, C. A. *Rep. Publ. Hlth med. Sub. Lond.* 1957, **98**, 43.

1. Berg, J. M., Brandon, G., Kirman, B. H. *Lancet*, 1959, ii, 441.

pupillary dilator) was studied in the same manner. Pupillary dilatation was recorded as millimetres of difference in size between the treated and untreated eyes. The results are summarised in tables I and II.

For each time-interval studied, and for both atropine and hydroxyamphetamine, 30 mongols show more millimetres of pupillary dilatation than do 30 non-mongol paired controls. Since atropine itself is not responsible for the observed difference in pupil response, one can only speculate on the reason for this difference between mongols and non-mongols.

Rainier School,
Buckley, Washington. JEAN H. PRIEST.

SIDEROSIS IN THE SOUTH AFRICAN BANTU

SIR,—At present, there is considerable interest in diseases and conditions characterised by iron excess. I would therefore be glad to be allowed to refer to certain aspects of the contribution by Golberg and Smith [1] on iron overloading and hepatic vulnerability.

In discussing the relevance of their experimental observations to human siderosis, they refer to siderosis in the South African Bantu. Regarding the ætiology of this phenomenon, they state, inter alia, " Gillman and Gillman [2] point to disordered metabolism of the hepatic cell; Walker and Arvidsson [3] draw attention to the heavy level of dietary iron. Both are partially correct. The amount of iron present in the liver is far too great to have arisen solely from disrupted mitochondria as the Gillmans assert, unless these mitochondria were loaded with iron in the first place; on the other hand, the dietary iron alone cannot adequately account for the enormously enhanced absorption from the intestine." As one responsible for the iron " overload " hypothesis on Bantu siderosis, I should like to challenge the latter part of this statement, and inquire upon what evidence their view is based.

First, regarding the amount of iron involved in siderosis in the Bantu, on the basis of Wainwright's [4] investigation in Durban, Bantu with *intense* siderosis (who incidentally form only a small percentage of Bantu siderotics) may gain about 10 g. excess iron over the period of say 10–20 years. This involves the accretion of 500–1000 mg. excess iron per annum, i.e., 1·5–3·0 mg. iron per diem. Now the balance studies of Fowler et al.[5] and of Gram and Leverton [6] show that iron intakes of the order ingested by the Bantu (up to 200 mg. iron per diem) are associated with absorptions far in excess of 1·5–3·0 mg. per diem. The findings in these studies are supported by recent investigations using radio-iron.

(1) Bothwell et al.,[7] in their observations on normal subjects given graded doses of iron, found that the mean amount of iron as ferrous salts absorbed ranged between 2 and 8 mg. as the dose was increased from 20 to 400 mg.

(2) Smith and Pannacciulli [8] summarised their recent investigation as follows: " Graded doses of iron from 0·001 to 300 mg., labelled with a tracer dose of Fe^{59}, have been given as a ferrous sulphate solution to subjects without anæmia and to patients with iron-deficiency anæmia, and the amount absorbed calculated from fæcal estimations. The mean absorption in the subjects without anæmia decreased from 33 per cent. of the 0·001 mg. dose to 12·6 per cent. of the 100 mg. dose, and in iron-deficient patients from 50 per cent to 37·5 per cent., respectively. No limit to the total amount absorbed was reached, the total increasing to 12·6 mg. and 37·5 mg., respectively, from the 100 mg. dose in the subjects without anæmia, and in the iron-deficient group. A further increase occurred when 300 mg. were given."

(3) The St. Louis workers, Brown, Dubach, and Moore [9] have investigated the extent of the block to iron absorption produced by large doses of inorganic iron given several hours before a tracer dose tagged with ^{59}Fe. The finding most specifically relevant to the South African Bantu is discussed as follows : " The degree of block to iron absorption demonstrated in normal subjects is certainly inadequate to prevent the absorption of unneeded iron from the diet. One would have little difficulty, for example, in explaining the large tissue iron accumulation in Bantu natives, whose diet has been estimated to contain as much as 200 mg. of iron per day. Using figures derived from our observations on normal subjects, a ' block ' in the Bantu would reduce absorption from an expected 34 mg. to 23 mg. This would still yield an increment of iron for shunting to storage depots of 22 mg. in excess of the adult male's estimated daily requirement."

The foregoing studies concern the short-term response to a high iron intake by white persons unused to such an occurrence. There is no corresponding information on the Bantu—another race and habituated for years to excessive ingestion of this element. One must be cautious, therefore, over extrapolation. Nevertheless, I submit that there is no evidence against the hypothesis that the high iron intake of the South African Bantu can account for the enhanced absorption from the intestine, and for the siderosis so common among these people. This does not imply that the high iron intake is the only factor involved.

I also wish to refer to the statement of Golberg and Smith that " of the factors which may be concerned in Bantu siderosis, a low protein diet suggests itself ". I am not aware of unequivocal evidence on humans that favours this view.

South African Institute
for Medical Research,
Johannesburg. ALEXANDER R. P. WALKER.

BLOOD-BARIUM AND MALIGNANT DISEASE

SIR,—Azevedo [1] reported that the barium content of the blood in cases of cancer varied between parts per million and parts per hundred thousand, whereas the normal level was higher and more constant. These observations were based on a spectrographic method of barium estimation. As this finding, if substantiated, offered the possibility of an early diagnostic test for cancer, and as no further reference to work in this field could be traced in the literature, we have checked these observations.

Using a different spectrographic technique, which will be reported elsewhere, blood from normal patients and from patients with clinically diagnosed cancer was examined. The tests were carried out on whole blood, as used by Azevedo, and extended to separate determinations on cells and plasma, in order to ascertain if there was any significant variation in the barium distribution.

In the early stages of this work sporadic contamination of the blood by barium was experienced. This was eventually traced to the lining of an electric muffle furnace and to an agate pestle and mortar, both of which had been used in the preparation of the blood samples for the spectrographic procedures.

The results obtained, once contamination had been eliminated, are shown in table I. These results differ from those of Azevedo in both level, constancy, and variation in disease. The distribution of barium between serum and cells is best shown by considering the ratio of barium concentrations in the serum and cells of individual samples. These results are summarised in table II. In normal blood the barium is mainly

TABLE I—BARIUM CONTENT OF BLOOD (μg. per kg.)

Range	No. of samples					
	Normal			Abnormal		
	Cells	Serum	Whole	Cells	Serum	Whole
0– 50	18	13	13	2	3	2
51–100	6	6	8	1	0	1
101–150	4	3	4	1	0	0
151–200	1	1	0	0	1	1
201–250	0	1	1	0	0	0
251–500	1	3	2	0	0	1
>500	1	1	0	0	4	1

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2. Gillman, J., Gillman, T. Perspectives in Human Malnutrition. New York, 1951.
3. Walker, A. R. P., Arvidsson, U. B. *Trans. R. Soc. trop. Med. Hyg.* 1953, **47**, 536.
4. Wainwright, J. *S. Afr. J. Lab. clin. Med.* 1957, **3**, 1.
5. Fowler, W. M., Barer, A. P., Spielhagen, C. F. *Arch. intern. Med.* 1937, **59**, 1024.
6. Gram, M. R., Leverton, R. M. *Fed. Proc.* 1951, **10**, 383.
7. Bothwell, T. H., Pirzio-Biroli, G., Finch, C. A. *J. Lab. clin. Med.* 1958, **51**, 24.
8. Smith, M. D., Pannacciulli, I. M. *Brit. J. Hæmatol.* 1958, **4**, 428.
9. Brown, E. B., Dubach, R., Moore, C. V. *J. Lab. clin. Med.* 1958, **52**, 335.

1. Azevedo, L. H. de P. *Acta Un. int. contra Can.* 1956, **12**, 409.

TABLE II—RATIO OF SERUM-BA/CELL-BA CONCENTRATIONS

Ratio range	No. of samples	
	Normal	Abnormal
<1	10	0
1–5	5	0
6–10	2	1
>10	1	2

found in the cells. In the abnormal bloods it is mainly in the serum.

It appears that the barium content of both the serum and cells from normal blood lies within the range 0–150 μg. per kg. and that the ratio of serum-barium to cell-barium should not be greater than 5 : 1. On the basis of the limited number of blood samples from cancer patients which we have been able to examine it is impossible to assess the utility of the blood-barium level as a diagnostic aid. Of the four abnormal samples on which we were able to obtain cell and serum barium concentrations, three fall outside the normal limits quoted.

We wish to acknowledge assistance from Dr. F. R. Wilde, Dr. T. A. J. Wickham, and Dr. G. M. G. Barton in the provision of blood samples.

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L. C. THOMAS
ROSEMARY A. CHITTENDEN.

INTRAHEPATIC TYPHOID INFECTION AS A CAUSE OF THE CARRIER STATE

SIR,—Removal of the gallbladder may relieve as many as 50% of chronic typhoid carriers. With the help of surgery, urinary carriers, under modern conditions, may be more easily dealt with.

Foci in the intrahepatic bile canaliculi are important, as Dr. Erlik and Dr. Reitler (June 4) show, but this fact was mentioned in earlier papers. For instance, Hobson [1] showed that these intrahepatic sites were important in mice. To be effective a drug must pass through the liver, with the bile, and be lethal for the infecting organism. Incidentally, sodium iodophthalein (' Opacol ') has had successes claimed for it in " clearing up " carriers.[2] Subcutaneous injections of a typhoid vaccine (T.A.B.) have been said to be helpful in these cases, but this is disputed.

Cholecystectomy alone holds out any prospect of cure (in 75%) according to one author,[3] who seems to have been forgotten. Sulphaguanidine is claimed by Loewenthal and Corfield [4] as almost a specific (to previous gallbladder removal they gave little credit). The combination of penicillin and sulphathiazole in large doses proved disappointing, though high concentrations of penicillin were demonstrated in the bile. On the other hand, Parker et al[6] were successful in 4 out of 6 cases given 3 million units of penicillin 6-hourly, reinforced by 1·5 g. probenecid twice daily, the course lasting ten days.

Pathological changes in the liver were described by Woolley [7] in a patient who had high-titre agglutinins in her sera. A sensitive test for the detection of chronic carriers is the Vi agglutination test as standardised by Felix. One of these resistant carriers—so-called " symptomless excreter "—can be a first-class medical problem, particularly if she (as nearly always) is a food-handler. It is advisable to make her swallow a " radio-opaque " Ryle's duodenal tube, and demonstrate, with X-rays, that the end of the tube is actually in the duodenum. Expert inspection may suffice, or a small barium " swallow " may help. With care, the tube will enter the duodenum within a few minutes (the overnight wait described by most authors is not always necessary). The gallbladder may be persuaded to contract by giving a fatty meal, by injecting 40 ml. of 33% watery magnesium sulphate down the tube, or by the intravenous injection of cholecystokinin (commercial preparation). A sample of bile is then aspirated and cultured. Two tubes [8] are not necessary nor is the large double-lumen tube [9] desirable. The sensitivity of the organism isolated is then tested with a series of antibiotics and drugs. Administration of the drug of choice can then be started, and specimens of bile obtained, by a similar manœuvre, on several occasions. The progress of the infection is easily watched; but not so easily controlled.

Among the remedies so tested could be included furaltadone (' Altafur '), a derivative of the chemical used with such success by Hobson.[1]

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FRANK MARSH.

CONTRASTING EFFECT OF CHLOROTHIAZIDE IN DIABETES INSIPIDUS AND PSYCHIC POLYDYPSIA

SIR,—In 1959 Crawford and Kennedy [10 11] observed that chlorothiazide and hydrochlorothiazide exert an antidiuretic effect in diabetes insipidus. In hypophysectomised, polydypsic, and polyuric rats, they noted a significant reduction of the water intake, whereas in patients with diabetes insipidus there was a considerable fall in the 24-hour quantity of urine. Recently we were able to test the effect of chlorothiazide in 4 patients with vasopressin-deficient diabetes insipidus. Our results fully confirm the observations of Crawford and Kennedy —namely, the water intake and the 24-hour urine volume decreased almost to half in all 4 patients and the specific gravity of the urine rose slightly. Analysing the Na, K, and Cl content of the urine we found that, though the concentration of the ions in the urine increased, the 24-hour Na and Cl output did not significantly change owing to the considerable drop in the amount of the urine, and only a slight hyperkaluresis ensued.

It seemed worth further examining the water metabolism of psychic polydypsic patients treated with chlorothiazide. It is known that this syndrome is associated with polyuria and polydypsia like diabetes insipidus; the patients pass urine of low specific gravity in abundant quantity. However, the polydypsia, in contrast to diabetes insipidus, is the primary change and the polyuria is simply the result of the increased water intake.

Examinations of three psychic polydypsic patients showed that chlorothiazide did not decrease the polyuria—on the contrary, corresponding to normal humans, such patients pass more urine. Similarly the Na, K, and Cl content of the 24-hour urine is also increased. In our opinion the different reaction to chlorothiazide in patients with diabetes insipidus and psychic polydypsia seems remarkable. After all, in both diseases antidiuretic hormone (A.D.H.) fails, but in diabetes insipidus A.D.H. production, in consequence of the lesion of the hypothalamo-neurohypophyseal system, ceases, while in psychic polydypsia, in the presence of normal functioning centres, the hypoosmosis inhibits the hormone mobilisation. The different response to chlorothiazide in the two conditions is so obvious as to be used for differential diagnosis.

What is the cause of the antidiuretic effect of chlorothiazide in diabetes insipidus, which otherwise increases the water and salt output? It cannot be the primary inhibition of the increased water intake because, in this case, the drug would

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2. Caile, R. *Brit. med. J.* 1943, i, 604.
3. Browning, C. H. *Spec. Rep. Ser. Med. Res. Coun., Lond.* 1933, no. 179.
4. Loewenthal, H., Corfield, W. F. *Brit. med. J.* 1943, ii, 105.
5. Fry, R. M., Jones, R. E., Moore, B., Parker, M. T., Thomson, S. *ibid.* 1948, ii, 295.
6. Parker, R. T., Fitzgerald, J. C., Perry, H. F., Woodward, T. E. *J. clin. Invest.* 1953, **32**, 593.
7. Woolley, E. J. S. *Brit. med. J.* 1954, ii, 623.
8. *Quart. J. Med.* 1958, **107**, 431.
9. Lageröf, H. O. *Acta med. scand.* 1942, suppl. 128.
10. Crawford, J. D., Kennedy, G. C. *Nature, Lond.* 1959, **183**, 891.
11. Kennedy, G. C., Crawford, J. D. *Lancet*, 1959, i, 866.

favourably influence the water metabolism of the psychic polydypsic patients too. Kennedy and Crawford [12] attribute the antidiuresis to tubular mechanisms.

Recently De Los Reyes et al.[13] stated that the chlorothiazide, in diabetes insipidus, leads to the reduction of the glomerular filtration-rate. We have also observed the decrease of the endogenous creatinine clearance in four patients with diabetes insipidus treated with chlorothiazide, and, like De Los Reyes et al., we think that the reduction of the glomerular filtration-rate may be related to the fall in diuresis. Our own observations on stalk-lesioned diabetes-insipidus rats also point to this: chlorothiazide led to a fall in urine volume and creatinine output. In other experiments [14] we have shown that in rats, which were hypophysectomised several weeks before and have a reduced glomerular filtration-rate, the diuretic and saluretic effect of chlorothiazide is less. After giving cortisone, however (when the glomerular filtration-rate rises) the effect of chlorothiazide on water and salt output is striking.

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MARGIT A. DÁVID
F. A. LÁSZLÓ
K. KOVÁCS.

"CUFF" HYPERTENSION

SIR,—In connection with the letters in your issues of July 2 and 16, the following incident may be of interest.

A child aged $6^1/_2$ years was under treatment at this hospital for severe tetanus, by curarisation and intermittent positive-pressure respiration, when one series of blood-pressure readings was made with a sphygmomanometer cuff containing a bag of only $10{\cdot}5 \times 5{\cdot}5$ cm. With this cuff the recorded readings rose from 110/70 to 160/110 mm Hg and until it was realised that the cuff was at fault hypercapnia was suspected. No clinical or biochemical confirmation of this was forthcoming, and the substitution of a cuff with bag $19{\cdot}3 \times 10{\cdot}8$ cm. gave readings again in the normal range. A subsequent test showed that the smaller cuff consistently gave results of some 35 mm. of the systolic and 25 mm. of the diastolic pressures above those given by the larger cuff. An "adult" cuff with bag 23×13 cm. gave results identical with those of the $19{\cdot}3 \times 10{\cdot}8$ bag. In every case the bag was centred over the artery. The mid-upper-arm circumference was 18·5 cm. with elbow extended and thus only the smallest bag was not able to embrace the arm completely. The arm muscles were, of course, fully relaxed at the time of the readings.

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SEROLOGICAL DIFFERENCE BETWEEN OLD AND YOUNG CELLS

SIR,—I read with considerable interest the preliminary report of Dr. Stratton and his colleagues (June 25). Both Brendomoen [15] and ourselves [16] had previously noted an agglutinin active against stored but not fresh red cells.

Our patient, like the patient of Stratton et al., was an elderly female with a hæmolytic anæmia associated with Hodgkin's disease. The serum of this patient when diluted 1 in 4000 would agglutinate the patient's own cells or cells of the same blood-group which had been stored for 72 hours at 4°C. The agglutinin was independent of the ABO and all the well-known blood-group systems and the agglutinability of the stored cells could be reversed by adenosine. This agglutinin differed from that reported earlier by Brendomoen in that it was most active at 37°C. In this and other respects, it seems to be identical with that reported by Stratton et al.

University of Virginia Hospital, Charlottesville, Virginia. C. HOUGIE.

12. Kennedy, G. C., Crawford, J. D. *Nature, Lond.* 1959, **184**, 1492.
13. De Los Reyes, M. P., Gomez, R., Bradford, I. *Lancet*, 1960, i, 650.
14. Kovács, K., Dávid, M. A., Horváth, I. W. *Arch. exp. Path. Pharmak.* 1959, **236**, 382.
15. Brendomoen, O. J. *Acta path. microbiol. scand.* 1952, **31**, 574.
16. Hougie, C., Dandridge, J., Bobbitt, O. B. Proceedings of 7th International Congress of the International Society of Blood Transfusion; p. 252. Rome, 1958.

Parliament

Mental Health (Scotland) Bill

ON July 12, at the committee stage of this Bill in the House of Lords, a Government amendment was accepted to ensure that the position of commissioner in the Mental Welfare Commission could not be held by a Civil Servant. This means that medical officers employed by the Department of Health for Scotland are barred, and there will thus be no doubt about the impartiality of the Commission in the exercise of its new duties to protect the interests of the patient.

QUESTION TIME

Deaths in Childbirth

Mr. KENNETH ROBINSON asked the Minister, in the light of the disclosure in his department's report on maternal deaths, 1955–57, that 41% of the 861 deaths expertly assessed were attributable to neglect and mismanagement and could have been avoided, what new steps he intended to take to protect the lives of women in childbirth.—Mr. WALKER-SMITH: I do not think that these figures carry quite the implication the hon. Member suggests. The report covers the second three years of a continuing investigation of the factors contributing to maternal deaths, and by promoting the study of those which are avoidable is itself an important contribution to the measures taken to bring about an improvement. I am glad to say that this second report contains ample evidence that a considerable improvement has in fact been achieved. Mr. ROBINSON: While the Minister can be congratulated on conducting this investigation, is he aware that his department's report is extremely disturbing in some respects? Would he not agree that, since the report also indicates that the risks attendant on childbirth in the home are about four times as great as those attendant on childbirth in hospital, it provides the most powerful argument for his implementing at an early stage the Cranbrook Committee's recommendations about more carefully and rigidly controlled obstetric lists?—Mr. WALKER-SMITH: The particular recommendation of the Cranbrook Committee which the hon. Gentleman has singled out is one which is under consideration in consultation with the medical profession. Most of the other recommendations in the Cranbrook report have already been commended to those providing the maternity services.

Dr. EDITH SUMMERSKILL: The Minister must not treat this so lightly. The report specifically states that domiciliary midwifery and midwifery in hospital can be severely criticised. On domiciliary midwifery, it states that a number of women who died in childbirth had heart-disease and nobody had examined their heart before the confinement. With regard to hospital midwifery, it is clear that people unfitted to do cæsarean sections in hospital have done them. I think that 140 women have died after a cæsarean section, which today should not be a complicated operation.—Mr. WALKER-SMITH: In so far as the report draws attention to avoidable factors, it does a public service, and we shall seek to ensure that those factors are avoided in future. At the same time, while resolute to progress in that way, we should keep the context in view. Over the period of three years covered by the report, over 2 million women were safely confined and, in this decade, we have succeeded in reducing the figures of maternal mortality from 0·87 per thousand in 1950 to 0·38 per thousand in 1959, a reduction of more than a half. These are figures which, I think, would arouse the envy and excite the emulation of most countries in the world.

Intake of Medical Students

Mr. L. A. PAVITT asked the Minister the number of full-time students entering university institutions for the first time in the faculty of medicine for 1954–55 and 1958–59; if he was satisfied that the current supply of newly qualified doctors was sufficient to staff the National Health Service.—Mr. WALKER-SMITH: According to my information, the number of students entering

medical schools in Great Britain was about 2100 in 1954–55 and about 1900 in 1958–59. The Willink Committee in 1957 suggested a reduction in student intake of about 10% as soon as practicable. The Royal Commission on Doctors' and Dentists' Remuneration last February expressed the view that the supply of candidates for training as doctors was reasonably close to requirements. Mr. PAVITT: Is the Minister aware that Professor Jewkes drew attention to the fact that this slowing down of the intake into the faculty of medicine could increase in momentum? Is he aware that, on the side of the G.P.s, a considerable amount of pressure is put on their time by large lists and that it is desirable to reduce the large lists to the size of the national average? Will not this require more doctors and not fewer?—Mr. WALKER-SMITH: The question of the size of lists raises rather larger issues. Of course, I have great regard for everything that Professor Jewkes says, but his was a minority report and the majority report said that the supply of candidates for training as doctors was reasonably close to requirements.

Mr. FENNER BROCKWAY: While the intake may be adequate for the medical service of this country, is there not a great need in Commonwealth countries, where, sometimes, there is only one doctor for 40,000 of the population?—Mr. WALKER-SMITH: Whatever may be the considerations affecting that, it clearly does not arise out of this question, which is limited to doctors " sufficient to staff the National Health Service ".

Outpatients and Consultants

Mr. WILLIAM GRIFFITHS asked the Minister whether he would instruct the Manchester Regional Hospital Board and the governors of the United Manchester Hospitals to take action in all outpatient clinics in hospitals under their control to make the patients aware of the identity of the doctor who sees them at the clinic.—Miss EDITH PITT replied: This is a matter for hospital authorities themselves to decide, in consultation with their medical staff. Mr. GRIFFITHS: Does the hon. Lady not think it undesirable that people who think that they will get the opinion of a distinguished consultant often do not see that consultant, although there may be very good reasons for that? What is even worse is that they have no idea who sees them. I think that they are entitled to know who is looking at their bodies and examining them.—Miss PITT: When the general practitioner names a consultant in the letter brought by the patient, normally that consultant will see the patient—— Mr. GRIFFITHS: That is not true at all.—Miss PITT:——but, to conserve time, his opinion may be conveyed in a letter from the registrar to the practitioner.

Dr. SUMMERSKILL: Does not the hon. Lady think that the Minister should make it clear to the hospitals that he does not wish these doctors always to wear a cloak of anonymity? The time has come when consultants must be told that they have no right under certain circumstances to allow their registrars to deputise for them. On the whole, most of them do fine work, but there is some evidence that there is too much deputising in some hospitals.—Miss PITT: There are occasions when a new patient may better be seen in the first instance by the registrar for history-taking and preliminary tests, but the final responsibility rests always with the consultant, and that is the point on which I want to reassure hon. Members.

Mr. GRIFFITHS asked the Minister whether he would give an assurance that patients referred by general medical practitioners to hospital outpatient departments to obtain an opinion of a doctor of consultant status, were not seen only by a junior doctor engaged upon his preregistration training.—Mr. WALKER-SMITH replied: It would not be appropriate for an outpatient to be seen only by an unsupervised, provisionally registered house-officer, and I have no evidence that this occurs. Some part of the investigation may properly be delegated to such junior staff under the consultant's responsibility. Mr. GRIFFITHS: Is the Minister aware that my information is that this sometimes happens in certain hospitals? If I send the details that have been provided to me, will he look into the matter and have it investigated?—Mr. WALKER-SMITH: Yes, of course, I will look at any case that the hon. Member likes to put to me. The principle is, however, as I have stated it in answer to the Question.

Mr. GRIFFITHS asked the Minister what procedure he was proposing to adopt in investigating the allegations of privilege accorded to private patients attending as National Health Service outpatients in certain Manchester Hospitals, details of which have been sent to him.—Miss PITT replied: I assume the hon. Member refers to the enclosures to his letter of July 6. These deal mainly with delegation of work by consultants to less senior doctors, but the Minister is arranging for consideration of this, and other matters with which he has been concerned, by the hospital boards.

Study Tours

Mr. KENNETH LEWIS asked the Minister how many representatives of the National Health Service would attend the International Hospital Federation study tour in the United States of America in September, 1960; how many of these representatives were being sent by regional hospital boards and how many by hospital management committees; and what was the cost to public funds or hospital free moneys.—Mr. WALKER-SMITH: 41 for England and Wales. 13 are being sent by regional hospital boards, 13 by hospital management committees, and 15 by boards of governors. The cost will be about £1100 to Exchequer funds and about £10,800 to non-Exchequer funds. Mr. LEWIS: I realise that these things are arranged through regional boards and management committees, but is the Minister not rather afraid that this might be the most expensive study tour since Caesar went to woo Cleopatra with all the support of the army medical corps and the apothecary services at that time? Does he not think that some control should be placed on these conferences, which are now inclined to be getting out of hand?—Mr. WALKER-SMITH: I rather think it was Antony, who had a larger establishment than Caesar, who was a very young man when he had his relationships. Also, of course, it is necessary to consider the change in the value of money over the 2000 years or so. I would not like to give a precise answer, but I assure my hon. Friend that this will be a very worthwhile exercise. I think that the people who go will have much that they can learn with profit from what they will hear and see. Dr. EDITH SUMMERSKILL: I thoroughly approve of the visit, but is the House to understand that legacies which have been left to hospitals by people who believed that their legacies would improve conditions in the hospitals and add to the amenities and so on will be used for this purpose?—Mr. WALKER-SMITH: The use of non-Exchequer funds is a matter for the individual hospital authority. It holds them as trustee and can use the funds as it thinks fit, subject to any specific trust, for any purposes which relate to hospital services.

Health Centres

Mr. W. W. HAMILTON asked the Minister of Health what steps he was taking to encourage the building of more health centres as envisaged in section 21 of the National Health Service Act, 1946.—Mr. WALKER-SMITH replied: I welcome local initiative in setting up health centres, especially in redevelopment areas and areas of large-scale new housing development, as I do the many other methods of bringing the different parts of the health service together. Mr. HAMILTON: Will the Minister not take the opportunity of deploring any restrictive tendencies which there might be in recently announced economic measures? Will he give an assurance that local authorities will not be hindered by those restrictive measures in their provision of such centres?—Mr. WALKER-SMITH: A number of health centres have been provided under section 21. In recent years loan sanction has been given in all cases where there has been local agreement to a health centre project, but the initiative in these matters must come from the locality concerned, and that involves a measure of agreement

among the general practitioners and otherwise before such a proposal is put forward.

Mrs. HARRIET SLATER: Will the Minister try to do a little more to convince practitioners that there is a useful service to be carried out and that they themselves would benefit from such a service which a local authority is able to give them in an efficient health centre.—Mr. WALKER-SMITH: I think that general practitioners are well aware of the desirability of grouped activities in one form or another, but they also proceed by way of group practice premises and by other methods. We were advised by the Guillebaud Committee to approach this matter on an experimental basis.

Group Practice Loans

The sum available to the Group Practice Loans Committee for 1960–61 is about £150,000. All of this has already been lent or promised, and the committee has decided not to consider further loans for the time being.

Prices of Proprietary Drugs

The Minister of Health has arranged with the Association of British Pharmaceutical Industry for a temporary extension of the Voluntary Price Regulation Scheme until Dec. 16 to allow further time for the review which he and the Secretary of State for Scotland are making of the experience gained during the trial period before arrangements for the future are settled.

Public Health

Byssinosis and Cotton-spinners

THE Industrial Injuries Advisory Council has unanimously reported to the Minister of Pensions and National Insurance that there are no grounds for extending the occupational cover for byssinosis under the Industrial Injuries Scheme to ring-room or mule-room workers in the cotton industry.

The Council, before reaching this conclusion, considered a report by the Nuffield Department of Occupational Health, Manchester University, which had been asked by the Minister to determine whether byssinosis exists among mule-spinners.[1]

Deaths in 1959

Provisional figures for numbers of deaths by cause in England and Wales last year are included in the Registrar General's first quarterly report for 1960.[2]

In 1959 deaths from acute poliomyelitis numbered 66, compared with 129 in 1958 and 226 in 1957; the 1959 total is the lowest since separate records were started in 1911. Deaths from ischæmic heart-disease continued to increase—from 76,324 in 1957 and 84,041 in 1958 to 84,920 in 1959, giving an annual death-rate of 1·87 per 1000 population. Deaths from cancer of the lung numbered 21,063 (18,181 male and 2882 female)—an increase of 1243 over the 1958 figure.

There were no deaths from diphtheria. Scarlet fever accounted for 1 death and whooping-cough for 25 deaths. Deaths from accidents involving motor vehicles numbered 6026, compared with 5439 in 1958 and 4898 in 1957.

The infant-mortality rate declined from 23·1 per 1000 in 1957 to 22·2 per 1000 in 1959.

Communicable Diseases

The latest edition of the American Public Health Association's handbook, *Control of Communicable Diseases in Man*,[3] deals with 111 diseases. The substance of the handbook has been accepted by the Ministry of Health and the Department of Health for Scotland with certain reservations to meet international commitments and agreements, and legal and administrative differences in the United Kingdom.

1. Cmnd. 1095. H.M. Stationery Office. 9*d*.
2. Registrar General's quarterly return no. 445. H.M. Stationery Office. Pp. 28. 2*s*.
3. Control of Communicable Diseases in Man. 9th edition, 1960. Obtainable from H.M. Stationery Office, P.O. box 569, London, S.E.1. 7*s*. 6*d*.

Obituary

ERNEST ROCK CARLING

Kt, M.B. Lond., LL.D. Belf., F.R.C.P., F.R.C.S., Hon. F.F.R.

As surgeon to the Westminster Hospital, dean of its medical school, and architect of its new building, Ernest Rock Carling accomplished what most people would consider a full life's work, and the Westminster was undoubtedly the centre of his career. But to him a centre was chiefly notable as a suitable starting-point for an ever-widening circle of service to his fellow citizens and to his own profession—officially as an adviser to Ministries, commissions, and trusts and as a chairman of scientific and charitable committees, and unofficially as a wise and experienced friend to his contemporaries of all ages.

He was born in 1877, the third son of F. R. Carling, J.P., and he was educated at the Royal Grammar School, Guildford, and King's College, London. While still a student at the Westminster Hospital he interrupted his hospital work to serve in the South African War with the Imperial Yeomanry Field Hospital. He returned to England to qualify in 1901. After holding hospital appointments and the demonstratorship in anatomy at the Westminster, he was appointed to the staff there.

Walter Stoneman

During the 1914–18 war he served in Belgium and France with the R.A.M.C., but apart from these years he worked at Westminster Hospital as surgeon, teacher, and administrator. He was a successful dean of the medical school, and he was responsible for much of the planning of the new buildings—particularly the arrangement of having complete units, comprising outpatients and inpatients, on the same floor. He also had much to do with setting up the radium centre there, and in 1929 he edited a *Course of Instruction in Radium Practice*. His gift for directing research and his special knowledge led to his appointment as a member of the Medical Research Council and of the Radium Trust.

At the beginning of the late war he was appointed consultant adviser to the Ministers of Health and of Home Security for the casualty services. After the war, because of his knowledge and experience of radiotherapy, he was asked to study the problems of protection against the hazards and risks of atomic weapons.

For the Government he wrote memoranda on civil defence, and his Harben lectures in 1956 were on ionising radiation and the public health. He was a member of the cancer and radiotherapeutic committee of the Ministry of Health; a member of the advisory committees on the Radioactive Substances Act and Atomic Energy Projects; consultant to the Ministry of Health, Home Office, and Ministry of Supply; and a member of the advisory panel of the Ministry of Labour and of the Advisory Committee on Nomenclature, Somerset House.

In the last years of the war and in the post-war years he shared in the work of many of the bodies that were concerned with the reorganisation of medicine. He took part in the Ministry of Health's survey of the hospital services. He became chairman of the medical advisory

committee of the new Central Health Services Council. He was a member of the executive of the Institute of Hospital Almoners. He had been a member of the Nuffield Provincial Hospitals Trust since 1942 and in 1946 he was appointed a governing trustee and the chairman of the medical advisory council.

Up to his resignation as a trustee in December, 1958, when he consented to serve as a special medical adviser to the Trust, he had taken a leading part in most of its projects. He was chairman of the Oxford Institute of Social Medicine, chairman of the advisory committee for the job analysis of hospital nurses, and a member of the controlling committee of the investigation into the function and design of hospitals. At the time of his death he was still an active member of the small steering group studying casualty services in England and Wales, whose report is now in the press.

He also was generous of his time and energy to the organisations of his own profession. He was a member of the committee of the Royal Medical Benevolent Fund, and a friend says that he "valued far more than all his distinguished offices that of treasurer of the Society for Relief of Widows and Orphans of Medical Men". One of his most important contributions was to the work of the Medical Protection Society, of which he had been president for the past 16 years.

He was knighted in 1944 for his war services. In 1945 he was elected F.R.C.P. under a special by-law. He was also an honorary LL.D. of the University of Belfast and an honorary F.F.R. Lady Carling died last year, and he is survived by two sons.

Sir Ernest died at his home in London on July 15. As these tributes from his friends and colleagues show, he was active and effective to the end.

To many generations of Westminster men and women he was always "Rockie Carling" or "Rockie" *tout court*, a designation which whilst embodying regard and affection was by no means devoid of admiration and respect; one in which he clearly delighted and retained even when in 1944 he became Sir Ernest. Adequately to sketch his career is to strain credulity that any one man could have undertaken so many obligations and displayed such ability and success in so many branches of human activity. His genius for construction and organisation was outstanding. For many years he toiled in the midst of his multitudinous obligations, as the dominating figure in the planning and creation of the new great Westminster Hospital and Medical School. There is not a stone in the structure that can have failed to absorb something of the spirit of his enthusiasm and ability when time and again he surpassed the professional architects on their own ground. Those who accompanied him in his long career always recognised how much Westminster Hospital meant to Rockie Carling. Now that he has passed on, future generations will realise how much Rockie Carling meant to Westminster Hospital.

A. A.

When he became an adviser to the Ministry of Health in the early days of the war Rock Carling was unfamiliar with the methods of a Government department, but his alert mind soon grasped procedure, while his tactful and friendly approach helped greatly in getting things adjusted. To his wisdom and forethought throughout the war much of the success of the Emergency Medical Services was due. Metaphorically, he made crooked ways straight and when a road seemed blocked devised a method of getting round it. He worked long hours, and under an appearance of calm and deliberation concealed untiring energy and devotion to the war effort. Short in stature, clean-shaven, with the eyes and brow of a deep thinker, he looked much younger than his real age. His loss will be keenly felt alike in the surgical world and in the vital sphere of endeavour to which he gave the last years of his life.

A. S. MACN.

Rock Carling was a man with breadth of vision, but in all his various works he never lost the personal touch. His memory of hospital staffs all over the kingdom was phenomenal; it was shown when just the right specialised opinion was required in Newcastle, Belfast, Birmingham, or wherever it might be. But more than that his contacts were truly kindly. In discussion of others he always tipped the balance in favour—a realist but also as someone wrote the day after his death "a very gentle gentleman". At the Medical Protection Society he showed his concern for the interest of those in difficulties; his grasp and breadth upon matters of major principle for the profession or the public; his wisdom and consistent kindness; and his care and thoughtfulness for the officers and staff of the society.

This year when the society moved to its new home in Hallam Street the council asked him to allow them to have his portrait painted: he agreed with great reluctance. When told that the members of council wished to make him a personal presentation to mark his twenty-first year among them he was amazed. It was proposed to make the presentation during the house-warming reception at which so many of his colleagues would be present, but he begged that it be made privately at an ordinary council meeting and it was felt necessary to respect his wishes. As one member said: "we put him on a pedestal but he was always getting off it".

His was a contribution to the civil and professional weal for which we are grateful. He died still fully working as he would have wished.

F. H. S.

As one of the small band of pioneers in the use of radium in the treatment of patients with neoplastic disease in this country, Sir Ernest Rock Carling became one of the founders of British radiotherapy. His work at the Westminster Hospital with the first teleradium units is part of the history of our specialty. In his later years he gave much of his time to the cause of radiation protection and to the safety both of those engaged in the handling of X rays and radioactive materials and of the innocent bystander.

Radiology has lost a friend, a tireless worker, and a forthright and sensible voice in the councils of several Ministries. He retained a remarkable capacity for the assimilation of detail, and for understanding new scientific and technical advances up to and past his 80th birthday. His sharp comments on foolish statements had a fine ring of authority to the very end. To those who knew him well the keen look from beneath those shaggy eyebrows and his precise, clipped speech warmed into a penetrating concern for their personal problems and welfare. An understanding man, acquainted with trouble and disappointment, he barely concealed a warm, generous, and kindly heart beneath his surface reserve. We shall be the poorer for the absence of this staunch supporter and most lovable man.

D. W. S.

It is over seven years since Sir Ernest Rock Carling became known to me as more than just the name of a man of eminence and influence. Much can be written of his intellectual capacity and the freshness and discipline with which, right up to the very end, he approached and mastered the most difficult and complicated subjects. Yet the future of humanity does not depend solely on power of intellect, and it seems to me that Sir Ernest's qualities of gentleness and kindliness which, with understanding, he showed to the most humble men and women, were equal pillars of his greatness.

G. MCL.

I knew Rock only during the last ten years of his life, but his small but impressive presence and quiet yet vivid manner made an immediate and lasting impression. Wherever he went he found old friends and made new ones, and, though he was as far as possible removed from what is called a ladies' man, I have heard three women of three different generations refer to him as "a darling"—and mean it. My memories of him will range over an exchange at theAthenæum of Boer War reminiscences with another 80-year-old doctor, his skill in allowing a man with a grievance to go on talking until a hostile mutiny

were so bored that they accepted the policy Rock Carling wanted, and his wise and kindly advice to a young Fleet Air Arm officer and a Chinese architectural student over the port at a Christmas dinner. *Exegi monumentum ære perennius.*

Although he had experienced several earlier intimations of mortality, he refused to allow his life or his work to be affected by them and he resented any attempt by his friends to lighten his heavy burden of committees and advisory posts: there was to be no retreat.

N. M. G.

It was a great privilege to be associated with Rock Carling in editing *British Surgical Practice*, for not only did I learn much from his own attitude to surgery and his approach to its problems through general medicine and applied science, but I also had the enjoyment of the friendship of a great man who was strong but gentle.

I suppose that as a surgeon he will be remembered chiefly for his contributions to the treatment of cancer by surgery combined with radiotherapy, but I had the opportunity of appreciating his real claim to be a general surgeon. We first met when Professor Gask took his unit to Westminster to see Rock Carling do an arthroplasty of the hip; and as we worked together for the past twenty years I have been constantly impressed by the prodigious width and depth of his experience and his knowledge of the evolution of surgery in the past fifty years. This enabled him unerringly to distinguish the true innovations from the rediscoveries, but he was characteristically careful to spare the feelings of a disillusioned " pioneer ".

He had a great love for the Royal College of Surgeons and enjoyed enormously his years as an examiner. In fact his last visit to the college was to attend the court dinner in May when he appeared as young and as full of vitality and enterprise as when he was an active member of the court. His mental vigour and his apparent freedom from physical disability made us forget his age, and his astonishing knowledge of advances in many fields of science and their application to medicine kept him a jump ahead of most of his juniors. As we planned together the subjects for the annual *Progress Volumes of British Surgical Practice* I never ceased to marvel at his understanding of modern developments and his familiarity with the men responsible for them.

His own surgical practice and his membership of the Pilgrim Surgeons and of the Association of Surgeons, as well as his work at the college, brought him into contact with all the leading surgeons at home and many of those abroad. The offices he held in the Emergency Medical Service and at the Home Office enlarged his acquaintance with medical administrators and those responsible for the services allied to medicine, in particular the scientists interested in protection against ionising radiations. He made use of these contacts in seeking authors for our articles, and in this way *British Surgical Practice* has been effective in fostering closer relationships between professional men throughout the Commonwealth. There is no doubt that Rock's warm heart as well as his clear head will ensure him a place among the Immortals.

J. P. R.

It can be said about E. R. C. that, having lived 83 years, he died as he would have wished—in harness. The very last day of his life he was one of the party to receive the University Grants Committee at his old medical school, and less than a week before he presided at a complimentary dinner to one of his colleagues and spoke with the ease and wit and charm of a man half his age. Were one to pick out the most outstanding feature of his intellect it would be that he was at least a quarter of a century ahead of his time. He perceived that the future of radiotherapy depended as much on the physicist as on the clinician. He mastered the intricacies of radiation physics before the unit of measurement was defined and he foresaw megavoltage before it was even thought of as a clinical concept. For the last few years protection against radiation hazards occupied much of his thoughts. He was an orthopædic surgeon before orthopædics became a recognised specialty.

He made friends for life, not always among those destined to success. He believed in the younger generation and supported them with an enthusiasm not often seen in his day. He rubbed shoulders with the great and was in-and-out of 10, Downing Street when Asquith was Prime Minister, and a generation later he was equally welcome in 11, Downing Street. He was a good companion and to travel with him—be it Italy where for many years he had a home, or Marie Curie and her colleagues in Paris, be it the great medical centres in Europe or the radioactive mines of Czechoslovakia—was an unforgettable experience.

Among the London surgeons of the past half-century he is one of the very few, perhaps half a dozen, who added something real yet intangible to the prestige of British surgery and did so more by his breadth of vision than by technique. He may have grown frailer in stature as the years rolled on, but never frailer in intellect or in the desire to put progress before everything else. He was in fact young to the very last, and those of us who knew him will think of him as he was to the end, clear of mind, young in spirit, eager to be in the front line of the advance of surgery and accepting till the very end the new in science as mandatory in the practice of medicine.

S. C.

DONALD ALDRIDGE MACPHERSON

L.R.C.P.E.

Dr. Macpherson, who died on June 14, had practised medicine on land and at sea, at home and abroad, among Servicemen and civilians, and inside and outside hospital. Everywhere he proved himself a good doctor and a kind and honest man.

After studying medicine at Charing Cross Hospital he took the Scottish triple qualification in 1911 and joined the White Star Shipping Company and served in the *Olympic*. In 1914 he joined the Royal Navy, and towards the end of the war he was seconded to the Royal Flying Corps. After the war he spent some ten years in general practice at Wolverhampton. He then joined the New Zealand Shipping Company and served for two or three years in the *Rangitaiki*. After this he obtained a licence to practise in Monte Carlo where he remained until 1940, when he escaped back to England on a coal boat. He made determined but unsuccessful efforts to rejoin the Royal Navy and finally persuaded the Army to accept him and joined the R.A.M.C. He first served at home and later he was in charge of an ambulance train in Belgium, based on Ostend.

On demobilisation he took a post at All Saints Hospital, Birmingham, for a short time and then returned to Monte Carlo; but he remained only a few months, for there was little work for an English doctor in the years immediately after the war. In 1946 he returned to All Saints Hospital.

F. E. D. G. writes: " I knew Mac for just over ten years, and my respect and admiration for him as a doctor and a man grew with each meeting. He had fine clinical judgment and precision, and often would read an accurate diagnosis through observation, without resort to extravagant radiological or pathological aid. Quite apart from medicine he was a delightful man. Varied clinical practice in many places had given him a sophisticated yet still sincere and simple attitude to life. He was old-fashioned in that he respected and displayed good manners. He was an aristocrat in the only meaning of the word that has any value—the power of quality. The latter years of his life were spent looking after the mentally sick, and to this work he brought all his clinical experience and human compassion."

WILLIAM MORTON

M.D. Glasg.

Dr. Morton, physician-superintendent of the City Hospital, Nottingham, died on July 9 at the age of 52.

He was educated at Glasgow High School and Glasgow University, qualifying in 1930. After holding house-appointments in Glasgow he became R.M.O. at Withington Hospital, Manchester. During the late war he served at home and overseas in the R.A.M.C., reaching the rank of lieut.-colonel in charge of the medical division of Chester Military Hospital.

In 1946 he was appointed medical superintendent of the City Hospital, Nottingham, and when the National Health Service started he became consultant physician to the City and Sherwood Hospitals. He was chairman of the East Midlands Old People's Welfare Committee, and he also served on the Sheffield Regional Hospital Board geriatric advisory committee and committee of rehabilitation. He was a founder member of the Medical Society for the Care of the Elderly (now the British Geriatric Society), and he was chairman of its executive committee from 1953 to 1956 and treasurer from 1954 to 1956. He was president of the Sheffield Regional Group of Occupational Therapists and treasurer of the Nottingham Medico-Chirurgical Society.

J. M. M. writes:

"During Dr. Morton's time in Nottingham many new departments in the City Hospital were completed, including a theatre block, outpatient and X-ray departments. He established an active occupational therapy department with one of the first rehabilitation kitchens in the country. In the days when a geriatric unit was something of a novelty he adapted two wards in the City Hospital as a treatment and assessment unit, and long-stay accommodation was provided in the nearby Sherwood Hospital. He also arranged a holiday service by which relatives could be relieved of the care of their sick old folks for a holiday spell. His original appointment as medical superintendent lost its administrative responsibilities when the health service started, but with the nominal title of physician-superintendent he retained the best of the personal functions of such an office. He took more than his share of committee work, particularly in relation to planning, and became a valued friend and adviser of his colleagues and of a host of others in and outside the hospital service. His manner was quiet and occasionally abrupt and he had a remarkably successful way of getting things done. As a clinician he was wise and knowledgeable."

Dr. Morton leaves a widow and three children.

Appointments

GIBB, A. G., M.B. Aberd., F.R.C.S.E., D.L.O.: senior E.N.T. surgeon, Eastern Regional Hospital Board, Scotland.
HALL, A. W. I., M.B. Cantab.: assistant M.O. and school M.O., Harrogate division, Yorkshire.
HANLEY, H. G., M.D. Lpool, F.R.C.S.: consultant urologist, Royal Masonic Hospital, London.
HEALEY, R. J., M.B. Sydney, F.R.C.S., M.C.R.A.: assistant radiotherapist (part-time M.O. status), St. Thomas's Hospital, London.
LAGOO, S. B., M.B. Poona: E.N.T. registrar, The Hospital for Sick Children, Great Ormond Street, London.
LAW, C. W., M.B. St. And., D.A.: S.H.M.O. in anæsthetics, Stornoway Hospitals.
WOOD, P. R. T., M.B. Lond.: assistant M.O., Horsham and Crawley area, Sussex.

Sheffield Regional Hospital Board:

JAMES, D. C., M.B. Lond., F.F.R., D.M.R.D., D.L.O.: consultant radiologist, Leicester area.
KAY, BRIAN, M.B. Sheff., F.F.A. R.C.S., D.A.: consultant anæsthetist, Derby area.
SIMPSON, KENNETH, M.D. Lond., M.R.C.P.: consultant pædiatrician, Leicester area.

Western Region Hospital Board, Scotland:

BARR, G. M., M.B. Glasg., M.R.C.O.G.: consultant obstetrician and gynæcologist, Renfrewshire area maternity service.
HARRINGTON, R. W., M.B. Glasg.: assistant ophthalmologist, Glasgow Ophthalmic Institution and Alexander Hospital, Coatbridge.
MCKECHNIE, SAMUEL, M.B. Glasg., F.F.A. R.C.S., D.A.: consultant anæsthetist, Greenock and district hospitals.
MACLEAN, D. G., M.B. Edin.: senior casualty officer, Alexandra Infirmary, Paisley.
PATERSON, M. L., M.D., B.SC. Glasg., M.R.C.O.G.: part-time consultant obstetrician and gynæcologist, Glasgow Royal Maternity and Women's Hospitals.
REID, H. C., M.B., B.SC. Glasg., F.R.C.S.E.: consultant surgeon, Victoria Infirmary, Glasgow.
SCOTT, L. S., CH.M. Glasg., F.R.C.S.E.: consultant surgeon, urological department, Glasgow Royal Infirmary.
TODD, N. A., M.B. Glasg., D.P.M.: assistant psychiatrist, Hawkhead Mental Hospital, Glasgow.

Colonial Appointments:

COOK, R. C., B.M. Oxon: M.O., Kenya.
GURNEY, J. M., M.R.C.S.: M.O., South Pacific health service.
HASTINGS, H. C., M.B. Edin., F.R.C.S.E.: surgeon/specialist, Jamaica.
HYATT, M. F., M.B. Lond.: M.O., Gambia.
PRINGLE, GORDON, M.D. Durh., D.T.M. & H.: director, East African Institute of Malaria and Vector-borne Diseases, East Africa High Commission.
WALKER, G. F., M.B. Lond., F.R.C.S.: orthopædic surgeon, Northern Region, Nigeria.
WHITE, R. H. R., M.B. Cantab., M.R.C.P., D.C.H.: M.O., Uganda.

Notes and News

CENTRAL HEALTH SERVICES COUNCIL

THE Minister of Health has appointed Mr. T. Holmes Sellors, Dr. Stanley Thomas, and Dr. Denis Hill to the Council for the period ending March 31, 1963. New medical appointments to standing advisory committees are:

Medical—Dr. A. B. Davies, Prof. T. McKeown, Mr. Holmes Sellors.
Nursing—Prof. R. C. Wofinden.
Mental Health—Dr. Mary Capes.
Cancer and Radiotherapy—Dr. E. F. Scowen, Prof. Andrew Semple, Prof. F. A. R. Stammers.

TIMETABLE FOR MENTAL HEALTH ACT

LAST week the Minister of Health explained the timetable for introducing the remaining provisions of this Act.[1]

Past

A start was made last October by bringing into force sections 1 and 149, which permit informal admission to designated mental hospitals. At the same time a review of certified patients already in hospital was begun, and some 26,000 had been de-certified by Dec. 31, 1959, when the review was far from complete. Many of these patients are remaining in hospital on an informal basis. Informal admission to mental-deficiency hospitals had started in January, 1958, under existing law, and by the end of 1959 well over half (about 35,000) of the patients in these hospitals had been de-certified and were receiving their treatment on an informal basis.

Local authorities have long had a duty to provide services for the subnormal; and soon after the Act was passed the Minister extended this duty to services for all mental patients, including for the first time the mentally ill. The local authorities have been asked to submit to the Minister their revised proposals for discharging this duty, and out of the 145 authorities in England and Wales all but 11 have now formally submitted proposals for approval.

Present

The local authorities were able to go ahead in this way under their general powers derived from the National Health Service Act. On July 15 section 6 of the Mental Health Act came into force; this removes any possible uncertainty about the scope of their powers. As a result of the Minister's direction authorities now have a duty to provide, equip, and maintain residential accommodation and training or occupation centres for mentally disordered persons, whether children or adults. They must also appoint mental-welfare officers, exercise their powers of guardianship when necessary, and provide ancillary or supplementary services.

The Act will introduce the single term "mental disorder" for all forms of mental illness or disability, and, as this term occurs in the sections on the local authority services, it was brought into use on July 15. The remaining definitions—severe subnormality, subnormality, and psychopathic disorder—will not be introduced until the parts of the Act in which they are used come into operation on Nov. 1.

Future

The chairmen of the Mental Health Review Tribunals, which are to be set up in each hospital region, will be appointed on Aug. 1, so as to be available for consultation by the Lord Chancellor and the Minister of Health during the final stage of preparation for the beginning of the tribunals' active work on Nov. 1.

Other provisions which will be introduced on that date include:

New procedures for compulsory detention in hospital or placing under guardianship, including rights of application to the tribunals;

Extension of powers of courts for dealing with mentally disordered offenders and mentally disordered juveniles in need of care or protection or beyond control;

1. See *Lancet*, July 16, 1960, p. 162.

Revision of arrangements under which the Court of Protection protects and manages patients' property;

New arrangements for registration of private nursing and residential mental homes;

Dissolution of the Board of Control.

THE DISCHARGED DEMENT

IN recent years, work with disturbed epileptics and with the severely subnormal has made cerebral damage and mental defect recede somewhat in importance as far as social disability is concerned; and environmental factors are believed more and more to lie behind many of the disturbances that such cases show. Apparently treatment and training can help the hopeless. Dementia paralytica, or G.P.I., is rarely seen these days, although when the diagnosis is made, there are now powerful therapeutic tools. Cerebral damage, nevertheless, cannot be repaired (two-thirds of discharged cases remain permanently demented) and the management of the stable post-G.P.I. defect poses considerable problems.

Miss M. H. Bree's interesting account [1] of the work of the Mott clinic at Horton Hospital, Epsom, shows how closely neurosyphilitic cases parallel other severely disabled people in their ability to live useful lives where social influences permit. The clinic, which had concentrated on the treatment, follow-up, and aftercare of G.P.I. since 1935, continued unchanged after 1948. Earlier work there had shown the prognostic importance of the previous personality, kind supporting relative, and some form of occupation (which should be within the person's capacity); and the present survey was planned to show in particular the effect of the patient on his immediate family. 275 out of 1200 cases seen between 1942 and 1952 presented adequate data plus continued survey over at least five years. (Follow-up by annual letter was found to give misleading information in at least three-quarters of this group.) 228 received aftercare of some kind. Only 11% were thought to have completely recovered; the rest were demented and 15% had multiple handicaps. Ages at discharge were between 40 and 60, men outnumbered women by 2 to 1, and about three-quarters were married. During the period of treatment and follow-up, about 1 marriage in 20 broke up, but the cause was usually thought unconnected with the venereal factor. Readmissions were surprisingly few and the large majority were managed adequately by their family: the general practitioner was little involved (only in 11 records were they noted as giving help), though whether this surprising fact is due to lack of interest or absence of need is not known.

Of the 275 patients, about 120 continued at their usual work and 65 were regularly employed but at a lower level. 18 were erratically occupied and 70 remained unemployed: about two-thirds of the total complained of pronounced financial stress, and 4 supporting relatives out of 5 changed to a parental role, especially the wives. This support was usually maintained with commendable affection and loyalty and only very rarely with a sense of martyrdom. Nevertheless in 103 families the demented member's presence was judged to have some clear adverse effect on the others; in 37 of the families there were young children. Community care is a double-edged weapon, and it is sometimes hard to be certain that we may not be doing more harm than good.

1. The Dement in the Community. By M. H. BREE, psychiatric social worker. With an introduction by Prof. Sir Aubrey Lewis. Horton Group Hospital Management Committee, Epsom, Surrey. 1960. Pp. 82. 2s. 6d.

University of Birmingham

Prof. Kenneth Mather, holder of the chair of genetics, has been appointed vice-principal of the university for five years in succession to Prof. G. W. H. Lampe.

Dr. Ian Bush has been appointed to the Bowman chair of physiology and to the directorship of the department of physiology from Oct. 1.

Dr. Bush, who was born in 1928, was educated at Bryanston School and at Pembroke College, Cambridge, and graduated with first-class honours in natural sciences in 1949. From 1949 to 1952 he was a Medical Research Council scholar at the Physiological Laboratory, Cambridge, and later at the National Institute for Medical Research, London. In 1952 he was awarded a Commonwealth fellowship and spent some months at the University of Utah and at the Massachusetts General Hospital. From 1953 to 1956 he was a part-time research assistant to the medical unit at St. Mary's Hospital, London, and from 1956 to 1958 graduate assistant to the regius professor of medicine at Oxford. In 1958 he became a member of the external staff of the Medical Research Council.

University of Manchester

At recent examinations the following were successful:

Ch.M.—Miles Fox.

M.B., Ch.B.—A. E. H. Emery, Edward Jackson, A. S. Tavill (honours); J. H. Ainsworth, Valerie Anderson, R. A. Appleton, Andras Barabas, Rosemary Barnes, Peter Bee, Barry Benster, M. M. Bluck, Maureen T. Boland, C. M. Bowkett, A. B. Brown, D. B. Clements, Claire Connors, J. L. Craven, A. C. Crompton, A. J. Crook, J. H. Earnshaw, G. A. Eccleston, Heather C. Ellwood, A. E. Fishburn, Alec Garner, G. R. Giles, J. A. Glass, Max Gringras, S. G. Hammersley, A. W. Hargreaves, J. B. Hobson, John Hodgkins, Jean M. Horrobin, Trevor Hughes, Geoffrey Ingram, S. M. Jackson, Sanjaye Jowaheer, M. F. Kilshaw, J. O. Lee, M. D. Lee, Anne K. Lumb, M. J. MacCulloch, Sylvia Manton, L. A. Michael, M. L. Neale, Margaret H. Ogden, R. S. Parker, H. V. Penketh, H. E. Porte, Pamela Proctor, G. N. Radcliffe, F. H. Ratcliffe, John Rhodes, D. I. Rushton, M. E. Serjeant, Mary S. Smith, Joan E. Speight, W. G. Staff, Jill Taylor, E. H. Thomas, Jack Tinker, Annie S. Tomlinson, M. R. Whittaker, Marian Whitwham, Margaret Wood, Jeanne M. Wright.

D.P.M.—Joseph Devlin, Constance M. Duddle.

D.P.H.—G. R. Brackenridge, E. J. H. Foster, Basil Gilbert, F. P. Peach, Beryl L. Sephton, Alan Sippert.

Royal College of Surgeons of England

At a meeting of the council on July 14, Sir Arthur Porritt was elected president and Sir Stanford Cade and Prof. Digby Chamberlain were elected as vice-presidents. Sir Clement Price Thomas, Mr. C. Naunton Morgan, and Mr. Hedley J. B. Atkins were readmitted as members of the council, and Mr. Humphrey G. E. Arthure was admitted as a coopted member of the council.

Dr. J. William Hinton (New York) was admitted to an honorary fellowship, and Prof. J. H. Louw (Cape Town) was admitted to the fellowship by election.

A Moynihan lectureship was awarded to Prof. J. F. Nuboer (Utrecht), and Dr. W. S. Stiles was appointed Edridge-Green lecturer. The Gilbert Blane medal for 1960 was awarded to Surgeon Captain C. P. Collins.

On Wednesday, July 27, at 5 P.M., at the college, Lincoln's Inn Fields, London, W.C.2, Dr. Zdenko Loewenthal, head of the department of medical history of the University of Belgrade, will give a lecture on the history of British-Jugoslav medical relations.

The council of the college has decided that the final phase in the programme of new building in Lincoln's Inn Fields will be named after the late Sir Archibald McIndoe. This part of the college will house the Hunterian Museum and a number of laboratories. At the Buckston Browne dinner at the college on July 13, the president, Sir James Paterson Ross, spoke of Sir Archibald's outstanding contributions to surgery and to the life of the college; and the council's intention to commemorate McIndoe's name in this way was warmly acclaimed. The President, who was replying to Mr. Julian Amery's toast of The College, referred appreciatively to the help the college had had from a number of devoted and enthusiastic industrialists and businessmen. Mr. A. Dickson Wright welcomed The Guests, for whom Mr. Harold Christie, Q.C., responded.

Royal College of Surgeons in Ireland

At a meeting on July 8, Mr. T. G. Wilson, the president of the college, inaugurated the new Faculty of Anæsthetists and conferred its honorary fellowship on Dr. John Gillies and Dr. G. S. W. Organe. The dean of the faculty is Dr. T. J. Gilmartin, and he and the other members of the first board of the faculty (see *Lancet*, May 7, p. 1034) were admitted as foundation fellows. The following were also admitted:

Sachindra Nath Basu, Kathleen Bayne, William Bingham, John Boyd, G. J. C. Brittain, D. G. Coleman, W. S. Davis, K. B. Glynn, T. F. Heavey, J. C. Hewitt, Margaret M. V. Lemon, J. A. MacAulay, Mary J. A. O'Connor, Margaret S. Deane Oliver, Frances E. Read, R. W. Shaw, M. A. Woods, J. D. Bourke, A. B. Bull, F. M. Byrn, A. H. Kasasian, O. V. S. Kok, Z. Lett, B. V. Lyne, P. R. Mesham, Maureen Murphy, D. L. Scott.

Institute of Disease of the Chest, London

Dr. J. R. Bignall has taken up the post of dean in succession to Dr. J. G. Scadding, who continues to be director of studies.

Royal College of Obstetricians and Gynæcologists

The opening of the new college building[1] last week was marked by a triple celebration. The Queen performed the official ceremony on the afternoon of July 13; next evening the Queen Mother attended a reception at the Senate House of London University; and a banquet was held at the Guildhall on July 15.

At the banquet Sir Edmund Stockdale, the Lord Mayor, said he was happy, as chief citizen, to pay his respects to a great profession; but he had grave misgivings about his capability of introducing their youngest into the world. Sir Andrew Claye, the president, spoke of the pride which all obstetricians felt in their new house; of their joy that the Queen had herself opened the building; and of their pleasure that so many old friends had shared in their rejoicings.

Prof. John Bruce, P.R.C.S.E., had come from behind the tartan curtain to bring good wishes "to the younger sister at her housewarming", and he was pleased that she was now established in a "decent little place". Mr. Donald Fraser proposed The Guests; and Mr. T. G. Wilson, P.R.C.S.I. responded.

Institute of Dermatology, London

A course in dermatology for medical registrars will be held on Thursday, Sept. 29, at the institute, Lisle Street, W.C.2. Applications should be made to the dean by Aug. 31.

National Spastics Society

On July 15 this society presented to Dr. E. R. Boland, dean of Guy's Hospital Medical School, the first £100,000 of the £2 million which it is raising to endow a chair and research unit in child health at the hospital.

Royal Free Hospital

On Wednesday, July 27, at 5.15 P.M., at the hospital, Gray's Inn Road, London, W.C.1, Dr. William B. Bean, of Iowa City, will speak on rare diseases: chronic atrophic polychondritis.

Hand Surgery

The Hand Club and the Second Hand Club will hold a meeting at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, at 10 A.M. on Saturday, Nov. 19. Papers from non-members will be welcomed. Further details can be had from Mr. H. Graham Stack, 150, Harley Street, W.1.

Committee to Study Health Education

A joint committee of the Central and Scottish Health Services Councils has been appointed under the chairmanship of Lord Cohen of Birkenhead to consider:

"whether, having regard to recent developments in medicine, there are any fresh fields where health education might be expected to be of benefit to the public; how far it is possible to assess the results of health education in the past; and in the light of these considerations what methods are likely to be most effective in future."

The other members are:

Central Health Services Council.—Prof. R. V. Bradlaw, dean and director of studies, Institute of Dental Surgery; Dr. H. D. Chalke, medical officer of health, Camberwell; Miss A. A. Graham, principal nursing officer, Northumberland; Dr. S. Wand, chairman of Council, British Medical Association.

Scottish Health Services Council.—Mrs. I. M. Allan, convener, Aberdeen Health and Welfare Committee; Dr. J. T. Baldwin, general practitioner.

Coopted.—Mrs. Mary Adams, deputy chairman, Consumers' Association, formerly assistant to the controller of T.V. programmes, B.B.C.; Mr. G. Cranch, research director, Messrs. Mather & Crowther, advertising agents; Miss M. Grieve, editor of *Woman*; Dr. G. R. Hargreaves, Nuffield professor of psychiatry, University of Leeds; Dr. E. Stephens, director of education, Glamorgan; Prof. R. C. Wofinden, medical officer of health, Bristol; Mr. S. Wynne, managing director, Voice and Vision, Public Relations.

Joint Secretaries.—Mr. W. N. Judd (Ministry of Health); Mr. A. W. Tait (Department of Health for Scotland).

The committee has decided that in the first place a limited number of bodies who are known to be directly connected with its work should be asked to submit evidence. Later, evidence from other interested bodies and persons will be invited.

1. See *Lancet*, July 16, 1960, p. 145.

Institute of Laryngology and Otology, London

Mr. J. C. Hogg has taken up the post of dean in succession to Mr. Chapple Gill-Carey.

Society of Medical Officers of Health

Dr. H. D. Chalke has been re-elected chairman of the council for 1960–61.

National Society for Mentally Handicapped Children

On July 13, Mr. Derek Walker-Smith, the Minister of Health, speaking at the conference held by this society in London, said that he looked forward confidently to the steady progress and gathering acceleration of the local-authority mental health services, but it would take time to evolve and elaborate all the services necessary for community care for the mentally handicapped. By the end of 1959 there were 293 whole-time and 59 part-time centres, providing for some 10,500 children, or about 80% of all suitable cases. But there remained 2600 children not receiving training in centres. Local authorities were considering plans for boarding accommodation where some children could stay during the week or for a term at a time. Some children now in hospital might be cared for as well, or better, in hostels. For those over sixteen years of age, there were at the end of 1959 42 whole-time and 28 part-time training centres which took nearly 7000, but there were as many again awaiting training.

Warley Hospital, Brentwood

On July 11 the Duchess of Kent opened the social centre which has been built at this hospital with a grant of £40,000 from King Edward's Hospital Fund of London.

The centre houses the social therapy department, the library, the hospital shop, and a patients' and visitors' tea lounge. The building is roughly Y-shaped, and a central foyer with the serving counter of the shop opens on the east side to a wing where there are offices for the doctor and therapist, two rooms for group activities, a kitchen for women patients, and changing rooms. There is also a small office for the editorial staff of the patients' magazine. To the south is large hall for physical training and social functions, and to the west are stairs leading up to the library and to a railed flat roof overlooking the cricket field, and down to the tea lounge, from which an open paved patio is reached through french windows. The architects are Messrs. F. W. MacKenzie & Partners.

Biological Engineering Society

The first meeting of this new society was held at the Royal College of Surgeons on June 10. It was attended by doctors, physiologists, electronic engineers, mechanical engineers, and physicists from many parts of the country. The purpose of the society is to bring together members of these different disciplines, from hospitals, research institutes, and industry, and to further the applications of engineering to biological and medical problems.

Dr. R. Woolmer, professor of anæsthesia at the Royal College of Surgeons, was elected first president. The acting secretary is Dr. A. Nightingale (physics laboratory, St. Thomas's Hospital, S.E.1), and other members of the council are: Dr. Philippe Bauwens, Prof. A. V. Hill, Dr. Guiseppe Pampiglione, Mr. W. J. Perkins, Mr. B. Shackel, Dr. N. Smyth, Dr. A. M. Uttley, Mr. H. S. Wolff, and Dr. B. M. Wright.

Sir Geoffrey Jefferson has been awarded the Fedor Kreuse medal of the Deutsche Gesellschaft für Neurochirurgie.

Prof. C. M. Fleming, under the sponsorship of the British Council, is visiting Poland and Germany.

Dr. Andrew Freier has been appointed assistant professor, Wayne State University College of Medicine, and assistant chief in obstetrics, Herman Kiefer Hospital, Detroit, Michigan, U.S.A.

Births, Marriages, and Deaths

BIRTHS

MICHELL.—On July 14 at the Middlesex Hospital, London, W.1, to Anne (née Pearce), wife of Dr. Guy Michell—a son (Johnathan), a brother for Christopher and Elizabeth.